Intracranial Germinoma Masquerading as Secondary Granulomatous Hypophysitis: A Case Report and Review of Literature

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Keywords

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Abstract

Germinomas are highly immunogenic tumors eliciting a strong peri-tumoral immune response that can spillover into the surrounding healthy tissues. This phenomenon can also occur in intracranial germinomas, manifesting as secondary hypophysitis. Herein, we report a case of 12-year-old-girl presenting with polyuria and polydipsia. She had central diabetes insipidus (CDI) and panhypopituitarism. Imaging revealed a sellar-suprasellar mass with infundibular stalk thickening. Transphenoidal biopsy revealed epithelioid granulomas with immunostaining negative for germinomatous cells. Other causes of hypophysitis were ruled out. Accordingly, she was diagnosed as primary granulomatous hypophysitis and treated with high-dose corticosteroids. Three years later she again presented with headache, vomiting and diminution of vision. Imaging showed a heterogeneous, solid-cystic peripheral rim-enhancing lesion at the same location with involvement of hypothalamus, ependyma and pineal gland. Cerebrospinal fluid beta-human chorionic go-

nadotropin was markedly elevated, confirming the diagnosis of an intracranial germ cell tumor. She was started on chemotherapy; however, she succumbed to febrile neutropenia. We performed a literature search and found 18 anecdotal cases of secondary hypophysitis associated with intracranial germinomas. There was a slight male preponderance (male:female 5:4). Two-thirds of the cases were below 18 years of age. Polyuria was the most common presenting manifestation (83%). CDI and panhypopituitarism were seen in 89 and 78% cases, respectively. Imaging evidence of pituitary stalk thickening was seen in 12 cases (67%), while pituitary enlargement and/or sellar mass were reported in 11 cases (61%). Pineal involvement was extremely rare, being reported in only 1 case, implying the predilection of suprasellar (rather than pineal) germinomas in causing secondary hypophysitis. Histologically, 82% had lymphocytic hypophysitis, while 18% had granulomatous hypophysitis. Initially, the diagnosis of germinoma was missed in 60% of the cases who were wrongly treated with corticosteroids. To conclude, physicians should make it a dictum that all children and adolescents presenting with CDI and pituitary stalk thickening should be rigorously screened for an underlying intracranial germinoma before labeling them as primary hypophysitis.

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Introduction

Central nervous system germinomas are rare, accounting for 0.1–3.4% of all primary intracranial tumors [1]. The median age of diagnosis is 10–12 years with a male predominance. They are usually negative (85–90%) for the commonly used tumor markers such as beta-human chorionic gonadotropin (β -hCG) and alpha-fetoprotein (AFP) [2]. Intracranial germinomas usually occur in the pineal recess (50–65%), sellar-suprasellar region (25–35%) and rarely in the basal ganglia/thalamus (5–10%) [3]. Bifocal tumors involving both suprasellar and pineal regions have been described in 6–41% of germinomas [4]. Pineal germinomas usually present with clinical features of intracranial hypertension and occasionally with Parinaud's syndrome. Sellar-suprasellar germinomas, on the other hand, tend to present with pituitary insufficiency (mainly growth hormone deficiency), diabetes insipidus (DI) and visual disturbances. Germinomas, as a cause of sellar-suprasellar mass, is however extremely uncommon. In a retrospective review of 2,598 patients by Faminini et al. [5] undergoing at least one pituitary magnetic resonance imaging, only 18% of the visible lesions were nonadenomatous lesions while all the rest were pituitary adenomas. Amongst the nonadenomatous lesions, Rathke's cleft cyst was most common, followed by craniopharyngioma and meningioma. Other rare sellar-suprasellar pathologies included metastases, hypophysitis and pituitary hyperplasia. Germinomas were identified in only 3 patients, emphasizing the rarity of this entity [5].

Hypophysitis is a rare condition characterized by inflammation of the pituitary gland and/or stalk, resulting in pituitary enlargement with or without hypopituitarism. Hypophysitis can be primary (most commonly lymphocytic, granulomatous, xanthomatous or necrotizing) or secondary (as a result of systemic diseases, immunotherapy or sella-based pathologies) [6]. Sellar/parasellar pathologies that can elicit secondary hypophysitis commonly include craniopharyngioma, Rathke's cleft cyst and pituitary adenomas [7]. Intracranial germinomas are also known to cause secondary hypophysitis. Anecdotal case reports of intracranial germinoma presenting as lymphocytic hypophysitis have been reported in world literature [8–21]. Rarely germinomas are also known to elicit a granulomatous reaction [22]. Hence, expectedly, granulomatous hypophysitis have also been reported in association with intracranial germinomas [23–25].

Herein, we report a case of a young girl presenting with central DI who was initially diagnosed as having granu-

lomatous hypophysitis and later found to be harbouring an intracranial germinoma. We have also reviewed all the hitherto published cases of intracranial germinoma and co-existing secondary hypophysitis.

Case Report

A 12-year-old-girl presented with the history of polyuria and polydipsia for the past 3 years. This was associated with nocturnal enuresis and an uncanny preference for ice-chilled water. She was evaluated at a local hospital and diagnosed as having central DI (CDI). She was started on desmopressin nasal spray and referred to our institute. Physical examination revealed a short, (height 137 cm, height SDS – 1.73), underweight (body mass index 14.4 kg/m²) and pre-pubertal child. Investigations revealed anaemia (haemoglobin 10.8 gm/dL), hypernatremia (serum sodium 146 mEq/L), normokalemia and normocalcemia. Work-up for polyuria, performed after stopping desmopressin for 24 h, revealed elevated serum osmolality (339 mOsm/kg) and low urine osmolality (87 mOsm/kg). Urine osmolality improved to 443 mOsm/kg after desmopressin challenge, suggestive of CDI. Anterior pituitary hormonal profile showed low free T₄ (0.57 ng/dL [range 0.7–1.8]), normal serum TSH (3.2 μ IU/mL [range 0.2–4.2]), low 800 h cortisol (60.8 nmol/L [range 171–536 nmol/L]), low serum adrenocorticotrophic hormone (4.2 pg/mL [range 5–65]), pre-pubertal levels of gonadotropins (LH <0.1 mIU/mL, FSH <0.1 mIU/mL) and elevated serum prolactin (43 ng/mL [range 4.8–23.3]). Serum cortisol reached a peak value of 256 nmol/L following parenteral administration of 250 μ g synacthen, confirming cortisol deficiency. She was immediately restarted on desmopressin nasal spray with which her polyuria improved and was also replaced with oral levothyroxine and hydrocortisone supplements. Subsequently, she underwent a contrast-enhanced magnetic resonance imaging of brain that revealed a homogeneously enhancing sellar-suprasellar mass, measuring 3.0 $\times$ 1.9 $\times$ 1.5 cm with infundibular stalk thickening. Posterior pituitary bright spot was not visualized. There was a separate pineal mass, measuring 6 $\times$ 4 mm showing similar intense homogenous contrast enhancement (Fig. 1a, b). Accordingly, a differential diagnosis of germinoma (considering the pineal lesion) versus hypophysitis (in view of stalk thickening) was kept. Her serum β -hCG and AFP levels were normal. Cerebrospinal fluid (CSF) analysis did not show any neoplastic cells. CSF β -hCG was slightly elevated (3.2 mIU/mL [normal value <3]), while AFP levels were normal (1.2 ng/mL [normal value <25]). Work-up for secondary causes of hypophysitis including contrast-enhanced computerized tomography (CT) of chest, ¹⁸F-FDG PET-CT, bone scintigraphy, serum angiotensin-converting enzyme level, anti-nuclear antibody, anti-neutrophil cytoplasmic antibody, syphilis serology and tuberculin skin test were all negative. She underwent transphenoidal biopsy that showed non-caseating compact epithelioid granulomas with multinucleated giant cells. Ziehl-Nelson stain did not show any acid-fast bacilli. Immunostaining for OCT4, placental alkaline phosphatase (PLAP) and β -hCG was negative (Fig. 2a–c). Accordingly, she was diagnosed as having primary granulomatous hypophysitis and started on oral prednisolone at a therapeutic dose of 1 mg/kg/day and hydrocortisone supplementation was stopped. An MRI repeated after 3 months of prednisolone therapy did not show any

Fig. 1. Contrast-enhanced MRI of the sella, coronal (a) and sagittal (b) views showing a homogeneously enhancing sellar-suprasellar mass (marked in blue arrow) with infundibular stalk thickening. The mass is seen compressing the optic chiasma (marked in red arrow). There is a separate small pineal lesion showing similar intense homogenous contrast enhancement (marked in yellow arrow).

Fig. 2. a Photomicrograph of the lesion showing multiple compact epithelioid cell granulomas separated by clusters of lymphocytes (H&E, $\times 350$). b Photomicrograph of immunohistochemistry of the lesion highlighting the CD20 positivity of the mononuclear cells scattered in between the compact granulomas (PAP, $\times 350$). c Photomicrograph of immunohistochemistry of the lesion showing negative staining, representing the staining carried out using OCT4, β -hCG and PLAP primary antibodies (PAP, $\times 350$).

reduction in size of the sellar-suprasellar lesion; hence, the possibility of intracranial germinoma was re-entertained. Repeat CSF analysis was still non-contributory. However, in view of non-response to glucocorticoid therapy, she was administered stereotactic radiotherapy targeting the sellar-suprasellar and the pineal le-

sions (total of 12 Gy). Prednisolone was tapered to a daily replacement dose of 2.5 mg while levothyroxine and desmopressin was continued. The plan was to repeat a MRI brain after 6 months and assess response to stereotactic radiotherapy. However, she was lost to follow-up.

Fig. 3. Contrast-enhanced MRI of sella, coronal (a) and sagittal (b) showing a heterogeneous solid-cystic peripheral rim-enhancing lesion in the sellar-suprasellar location. It is seen involving the hypothalamus, pars intermedia along with diffuse enhancement of the ependyma and the pineal gland.

She presented to us 3 years later in November 2016. She had developed persistent headache, recurrent vomiting, diminution of vision in both eyes and altered behaviour since July 2016. A CT scan at a local hospital showed a hyperdense mass in the sellar region with associated hydrocephalus. A right-sided ventriculoperitoneal shunt was placed, following which her headache and vomiting reduced, but, the other symptoms persisted. Hence she was again referred to our institute.

On examination, she was drowsy but arousable. She was counting fingers from a distance of 1 m in both the eyes. She had bilateral vertical nystagmus with the fast component being directed upwards. Fundoscopy showed bilateral disk pallor suggestive of optic atrophy. Investigations revealed persistent hypernatremia (serum sodium ranging between 150 and 157 mEq/L), normal T₄ (8.1 µg/dL [range 4.2–12]), low 800 h cortisol (137 nmol/L) and pre-pubertal gonadotropin levels. She had polyuria and elevated serum osmolality (371 mOsm/kg) even on desmopressin nasal spray (20 µg/day). Repeat contrast-enhanced magnetic resonance imaging showed a heterogeneous solid-cystic peripheral rim-enhancing lesion at the same location. It was now involving the hypothalamus, pars intermedia along with diffuse enhancement of the ependyma and the pineal gland (Fig. 3a, b). There was no imaging evidence of spinal cord involvement. Repeat analysis of CSF showed highly elevated β-hCG (273.3 mIU/mL). Knitting the typical imaging finding of ependymal spread and elevated CSF β-hCG, she was diagnosed as having primary intracranial germ cell tumor with secondary granulomatous hypophysitis. She was started on bleomycin, etoposide and cisplatin-based chemotherapy and planned for sequential craniospinal radiotherapy. However, after the first cycle of chemotherapy, she developed febrile neutropenia and succumbed to multidrug-resistant *Escherichia coli*-related sepsis. Autopsy could not be done as the patient's family did not consent for this procedure.

Review of Literature

We performed an extensive literature search in PubMed, EMBASE and SCORPUS using the terms “germinoma and hypophysitis,” “germinoma and stalk thickening,” “germinoma and autoimmunity” and “germinoma and granulomatous reaction.” We came across 18 cases reported in English language over a period of 21 years (1999–2019; Table 1). Most of the reported patients were male (male:female = 5:4) with an age range of 6–45 years. Two-thirds of the cases were below 18 years of age highlighting the preponderance of intracranial germinomas in the first 2 decades of life [26]. The most common presenting manifestation was polyuria (83%) while mass symptoms in the form of headache and visual complaints were seen in about 56% of cases. Growth failure, pubertal delay, secondary amenorrhoea, galactorrhoea, fatigue and loss of appetite were rare concurrent presenting symptoms. Investigations revealed CDI as the most consistent hormonal abnormality (89%). Multiple pituitary hormone deficiency (comprising of ≥3 anterior pituitary hormones) was present in 78% of the cases, while elevated prolactin levels (basal or TRH-stimulated values) were reported in 50% of the cases. Associated autoimmune disease (type 1 diabetes mellitus) was reported in one case [18]. Imaging evidence of pituitary stalk thickening was seen in 12 cases (67%), while pituitary enlargement and/or sellar mass was reported in 11 cases (61%). Isolated stalk thickening without any radiological sellar – suprasellar involvement was reported in 6 cases [11, 14, 17–19, 21]. Pineal involvement was reported in only one case [18] implying the predilection of suprasellar (rather than pineal) germinomas in causing secondary hypophysitis. Absence of posterior pituitary bright spot, hypothalamic and cavernous sinus involvement were infrequently reported. Interestingly, the patient reported by Bettendorf et al. [8] had a normal sellar imaging at the time of presentation. After a period of 2 years, she developed pituitary stalk thickening that remained stable over the next couple of

Table 1. Eighteen cases of intracranial germinoma associated with secondary hypophysitis hitherto reported in world literature

Serial No. [reference]	Age/ gender	Clinical presentation	Hormonal work-up	MRI brain findings	Tumoral markers	Pathological subtype of hypophysitis	Initial treat- ment
1 [8]	8/F	Polyuria	CDI, panhypopit, TRH-stimulated elevated Prl	Initially normal Later enlarged pituitary and thickened stalk	Serum PLAP, β -hCG, AFP negative	Lymphocytic hypophysitis	GC
2 [9]	6/F	Polyuria	CDI, panhypopit, TRH-stimulated elevated Prl	Enlarged pituitary, and thickened stalk	Serum PLAP elevated (later stage)	Lymphocytic hypophysitis	GC
3 [10]	45/M	Headache, extra-ocular mus- cle palsy	Low LH, FSH	Sellar mass extending into right cavernous sinus	CSF β -hCG elevated	Lymphocytic hypophysitis	GC
4 [23]	12/M	Visual field defects, polyuria, fatigue, anorexia	CDI, panhypopit	Intrasellar mass with supra and right parasellar extension	Serum β -hCG, AFP normal	Granulomatous hypophysitis	GC
5 [11]	13/M	Polyuria, visual field defects	CDI, panhypopit	Thickened stalk	ND	Lymphocytic hypophysitis	Surgery
6 [11]	21/M	Polyuria, visual field defects	CDI, panhypopit	Pituitary infiltration and thickened stalk	ND	Lymphocytic hypophysitis	Surgery
7 [12]	24/F	Headache, menstrual distur- bance	Low T4, LH, FSH, elevated Prl	Sellar mass and thickened stalk	CSF β -hCG normal Serum β -hCG elevated	Lymphocytic hypophysitis	GC
8 [13]	13/F	Headache, polyuria, arrested puberty	CDI, Low fT3, fT4, FSH, LH, poor GH response to arginine	Enlarged pituitary gland, mass lesion in the pituitary stalk and inferior hypothala- mus	Serum and CSF β -hCG normal Serum AFP normal	Lymphocytic hypophysitis	GC
9 [14]	12/F	Growth retardation	CDI, panhypopit	Thickened stalk	ND	Lymphocytic hypophysitis	GC
10 [24]	13/M	Polyuria, headache, anorexia	CDI, panhypopit, elevated Prl	Intra and suprasellar mass with right parasellar extension	Serum β -hCG, AFP, CEA, PLAP normal	Granulomatous hypophysitis	RT
11 [15]	18/F	Polyuria, delayed puberty	CDI, panhypopit, elevated Prl	Thickened stalk, enlarged pituitary, cystic mass in inferior hypothalamus	Serum β -hCG, AFP normal	Lymphocytic hypophysitis	GC
12 [16]	11/F	Polyuria, growth retardation	CDI, panhypopit, elevated Prl	Intra and suprasellar mass, extending into hypothalamus	Serum β -hCG, AFP normal	Lymphocytic hypophysitis	GC
13 [17]	10/M	Polyuria, growth retardation	CDI, panhypopit	Thickened stalk, tuber cinereum nodule Absent PPBS	Serum β -hCG, AFP, CEA normal (initially) Later serum and CSF β -hCG elevated	Lymphocytic hypophysitis	CCT, RT
14 [18]	10/M	Polyuria Later growth retardation and Parinaud syndrome	CDI, panhypopit	Thickened stalk, absent PPBS, later pineal cyst	Serum β -hCG, AFP normal CSF β -hCG elevated	NA	RT
15 [19]	24/F	Polyuria, fatigue, galactor- rhea, amenorrhoea	CDI, panhypopit, elevated Prl	Thickened stalk, normal sella	Serum and CSF β -hCG, AFP normal	Lymphocytic hypophysitis	CCT, RT
16 [25]	17/M	Polyuria, headache, dimini- tion of vision	CDI, Low cortisol, LH, FSH, elevated Prl	Large suprasellar lesion with solid-cystic components	ND	Granulomatous hypophysitis	Surgery, RT
17 [20]	26/M	Polyuria, headache	CDI, panhypopit, elevated Prl	Sellar mass and thickened stalk	CSF β -hCG, AFP normal	Lymphocytic hypophysitis	GC
18 [21]	26/M	Polyuria, diminution of vision	CDI	Thickened stalk	NA	Lymphocytic hypophysitis	GC

F, female; M, male; CDI, central diabetes insipidus; panhypopit: panhypopituitarism; Prl, prolactin; TRH, thyrotropin-releasing hormone; FSH, follicle-stimulating hormone; CSF, cerebrospinal fluid; PLAP, placental alkaline phosphatase; β -hCG, beta-human chorionic gonadotropin; AFP, alpha-feto protein; CEA, carcino-embryonic antigen; GC, glucocorticoid; CCT, chemotherapy; RT, radiotherapy; NA, not available; ND, not done.

years. Thereafter, MRI revealed pituitary enlargement and further infundibular thickening with subsequent impingement on the optic chiasma.

Data on serum and CSF tumor markers are highly variable and discordant. In most of the cases, serum β -hCG and/or AFP were reported as normal [8, 13, 15, 16, 18, 19, 23, 24]. CSF β -hCG and/or AFP were elevated in a few [10, 17, 18] and normal in the rest [12, 13, 19, 20]. Surprisingly, Ozbey et al. [12] had reported a case where the CSF β -hCG was normal while the serum level was elevated. Just like evolution of radiological features, sero-conversion of serum β -hCG has been occasionally reported [17]. Data on serum PLAP are all the more scarce with only 3 cases reporting serum PLAP levels [8, 9, 24]. Histological confirmation of hypophysitis was made in all but 1 case [18]. Fourteen patients were initially labeled as having lymphocytic hypophysitis, while only 3 had granulomatous hypophysitis [23–25]. Although the diagnosis of intracranial germinoma was ultimately clinched in all the patients, about 60% of the patients were initially treated with glucocorticoids with little or no improvement in clinical and radiological features.

Discussion

We have described a case of a young girl who had presented with CDI, growth failure and pubertal delay. MRI showed a sellar-suprasellar mass, pituitary stalk thickening and a sub-centimetric pineal lesion. Transphenoidal biopsy was suggestive of granulomatous hypophysitis and tissue markers for germinoma were all negative. Considering the pineal lesion and elevated CSF β -hCG value (even though only slightly), a possibility of an intracranial germ cell tumor was definitely entertained; however, the pathological report was given undue precedence and she was treated initially only with high dose glucocorticoids. As there was no clinical or radiological response, she received stereotactic radiotherapy in the interim period, again keeping in mind the possibility of an intracranial germinoma. Perhaps a full-fledged craniospinal radiotherapy with tumor boost or at least whole ventricular radiotherapy would have been the treatment of choice at that point of time. We can however assume that our “half-hearted attempt” of stereotactic radiotherapy could have led to transient “stunning” of the germinoma as she remained stable over the next 3 years and refrained from any sort of medical attention. However, she soon became symptomatic when imaging showed a large solid-cystic suprasellar mass with diffuse ependymal involvement, a feature characteristic of intracranial germ cell tumors [27]. At this time, CSF β -hCG was unequivocally elevated, enabling us to make a diagnosis of an intracranial germ cell tumor. A delay of 3 years with suboptimal treatment might have led to a malignant transformation from

a “pure germinoma” (with little β -hCG secretion) to a non-germinomatous germ cell tumor (with abundant β -hCG production) and extensive intracranial spread. Such a phenomenon of spontaneous transformation of germ cell tumors is well-known [28, 29].

Primary autoimmune (lymphocytic) hypophysitis is primarily a disease of females, mostly in the peri-partum period [7]. It is a rare occurrence in children and adolescents. Gellner et al. [30], in their 2007 review, could find only 25 cases of lymphocytic hypophysitis. Of these 25 cases, 4 patients actually had secondary hypophysitis consequent to an intracranial germinomas [8, 9, 11, 13]. On the contrary, the prevalence of hypophysitis in adults is about 0.24–0.88% [31]. When 170 consecutive adult patients of hypopituitarism and/or central DI were screened for the probable etiology, 23 (13.5%) were found to have primary hypophysitis [32]. Primary granulomatous hypophysitis, another variant of autoimmune hypophysitis, is all the more rare in the pediatric and adolescent age group. A systematic review of 82 cases of idiopathic granulomatous hypophysitis by Hunn et al. [33] showed that the median age at presentation was 44.4 years with only 5 cases (6%) belonging to the age group of 10–19 years. With this background, the pre-test probability of a primary granulomatous hypophysitis was already low in our patient. Hence, all possible secondary causes of granulomatous hypophysitis were investigated for and duly excluded. As the transphenoidal biopsy did not show any atypical/germinoma cells, the diagnosis of granulomatous hypophysitis secondary to an intracranial germinoma was excluded.

Germinomas are characterized by the presence of large cells, each harboring a centric nucleus with one or more prominent nucleoli, surrounded by a clear and abundant cytoplasm. The cells typically stain positive for PLAP, c-kit protein (CD117) and OCT 3/4. In addition, the tumor contains numerous infiltrating lymphocytes. In most cases (75%), infiltrating lymphocytes are seen co-existing with nests of neoplastic cells, establishing a 2-cell pattern. In the rest (25%), lymphocytes largely outnumber the few scattered neoplastic cells, thereby making it difficult to make a histopathological diagnosis of germinoma [34].

Germinomas are highly immunogenic tumors, able to elicit a strong peri-tumoral autoimmune response. It is hypothesized that germinoma cells express a wide range of antigens, some of them being neo-antigens to which the host immune system has never been exposed to, thereby initiating a polyclonal autoimmune reaction. Such a hypothesis has been substantiated by the fact that antigens on germinoma cells are recognized by patient's

own serum. The resulting autoimmune response leads to recruitment of immune cells (especially lymphocytes) at the site of the germinoma. Once homed to the tumor site, the immune cells could then spill over to the neighboring tissues (infundibulum and/or pituitary gland), causing radiological and clinical abnormalities [16]. Our patient was mostly likely harboring a bifocal tumor at both pineal and suprasellar sites with the suprasellar component most likely responsible for the secondary hypophysitis which was inaccessible via the transphenoidal route.

The underlying pathophysiological differences that dictate the differential development of lymphocytic versus granulomatous hypophysitis in response to an intracranial germinoma are still a matter of speculation. Lymphocytic hypophysitis, in general, is characterized by an abundance of CD4+ T-helper cells (Th cells) and CD20+ B-cells [35]. The CD4+ T-cells are predominantly of the Th2 subtype. Th2 cells produce cytokines (interleukin 4) that activate B-cells. Granulomatous hypophysitis, on the contrary, contains a majority of cytotoxic T cells (CD8+) and histiocytes [35]. The predominant CD4+ T-cell subtype is Th1 that produce interferon- γ which activates CD8+ T-cells and macrophages, thereby eliciting a type IV hypersensitivity reaction and promoting granuloma formation. The abundance of local infiltrating Tregs (regulatory T-cells) has also been proposed as a plausible mechanism for granuloma formation [36]. It can be assumed that germinoma cells might be expressing a myriad of antigens that can either activate the Th1 or Th2 pathway, thereby eliciting a granulomatous or lymphocytic response, respectively. In vitro studies with cultured germinoma cells might help resolve this question.

The overwhelming immune response with a tendency to spill over into the surrounding tissues may enshroud the underlying germinoma. An attempt to access the target lesion via endoscopic approach may lead to erroneous sampling from the periphery of the lesion, an area where the immune cells are in abundance. This would lead to a misdiagnosis of lymphocytic or granulomatous hypophysitis and divert all the attention of the physician away from the underlying culprit neoplastic lesion. Such was the scenario in our case. Mueller et al. [37] have discussed the diagnostic dilemmas encountered in intracranial germinomas with a peripheral granulomatous response. They have concluded that an open biopsy approach should be preferred over endoscopic or stereotactic surgery in a midline lesion with strong clinical suspicion of germinoma. However, if open biopsy is not feasible or contraindicated by the clinical scenario, stereotactic or endoscopic approach can be adopted and multiple sam-

ples should be obtained from several different target points within the lesion to avoid sampling error [37].

The need to differentiate primary autoimmune hypophysitis and secondary hypophysitis consequent to an underlying intracranial germinoma has direct repercussions on management strategies. Primary hypophysitis responds to glucocorticoid therapy, marked by resolution of pituitary enlargement and stalk thickening with or without improvement in the adenopituitary hormonal status [7]. Non-response to standard treatment regimen should make the physician think about secondary causes of hypophysitis with intracranial germinomas being a strong differential diagnosis, especially in children and adolescents.

Conclusion

In conclusion, intracranial suprasellar germinomas can present with clinical and radiological features indistinguishable from primary hypophysitis. Endoscopic or stereotactic approach may not be adequate to access the culprit lesion. Misdiagnosis as primary hypophysitis usually leads to inadvertent treatment with glucocorticoids. Hence, as a dictum, germinoma should be suspected in all children and adolescents presenting with CDI and pituitary stalk thickening with or without other pituitary hormone deficiencies.

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Author Contributions

R.P. is the primary author and had managed the index patient at the second admission. K.V. helped procure the histopathological images. A.R. and Prakamya Gupta helped perform literature

search. P.G. had managed the index patient at the first admission. (Late) K.K.M. had performed transphenoidal biopsy of the index patient. P.S. and N.R. helped procure the radiological images. A.B. edited the manuscript. P.D. helped perform literature search and provide overall guidance.

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