CNS GERMINOMA WITH SYNCHRONOUS LESIONS IN THE SUPRASELLAR AND PINEAL REGIONS: CLINICAL, CT AND IMMUNOLOGICAL FOLLOW-UP

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ABSTRACT

Germinomas are the most frequent type of germ cell tumors that constitute only 2-5% of all central nervous system malignancies. Most of them arise in the pineal and suprasellar regions but in about 5% to 10% the simultaneous location is found. Although their strategic location, they respond well to surgery, radiation and chemotherapy and the prognosis is very good. We report a case of 23-years young male presented with gait disturbance, weakness in lower extremities, visual impairment and moderate fatigue. His medical history revealed that he was symptomatic by DI (polyuria, polydipsia and weight loss) and received treatment with adiuretin for a period of 3 years. Computed tomography (CT) scans demonstrated well circumscribed tumor lesions with a homogeneous contrast enhancement in the suprasellar and pineal regions. A germinoma was verified histologically. A good treatment response to surgery, radiation, chemotherapy and management of endocrine insufficiency was achieved. The post-operative neurological, CT and immunological follow-up corresponded with the clinical course of the disease and the results of therapeutic procedures.

Key words: germinoma, synchronous location, clinical presentation, CT imaging, immunological monitoring

INTRODUCTION

Germinomas are the most common intracranial germ cell neoplasms, accounting only 2-5% of all CNS malignancies [3, 11, 17]. They are most likely found in younger patients (between 10 and 30 years old) with a peak incidence at puberty, suggesting a hormonal influence [8]. Intracranial germinomas occur with a strong male predominance and approximately 95% are found in the midline, in the pineal (65%) and suprasellar (about 25%) regions [15, 21, 29]. The most common symptoms are related to their location, size and speed of growth. The diagnosis is based on the typical clinical expression, contrast-enhanced CT/MRI, specific endocrine and other lab tests [2, 3, 14, 17, 21, 29]. The differential diagnosis of germinomas includes both

neoplastic and non-neoplastic processes such as pituitary adenomas, craniopharyngiomas, true pineal tumors, gliomas, meningiomas, metastatic tumors and vascular anomalies [2, 11, 21, 29]. The overall treatment of germ cell tumors involves surgery, radiation, chemotherapy and management of endocrinopathies. A review of the literature shows that simultaneous pineal and suprasellar germinomas may be found only in 5% to 10% of all germ cell tumors [10, 11, 28]. Although rare, they represent an important diagnostic and therapeutic challenge because of the strategic location, broad spectrum of clinical symptoms, and immunosuppression.

CASE PRESENTATION

A 23-years young male was admitted to the hospital with clinical features of gait disturbance, weakness in lower extremities, visual impairment and moderate fatigue. The past medical history revealed that he became symptomatic by DI (polyuria, polydipsia and weight loss) and received treatment with adiuretin for a period of three years. Neurological examination found only signs of truncal and gait ataxia, as well as decreased visual acuity while physical one was normal. Initial CT scans demonstrated synchronous tumor lesions with a homogeneous, intense contrast enhancement in the suprasellar (diameter 16 mm) and pineal (diameter 20 mm) regions (Fig. 1). One month later the tumor in the suprasellar region was subtotally removed. The histological investigation confirmed a germinoma and the patient underwent radiotherapy (total dose of 47.2 Gy in the sellar region). The CT scans after surgery and irradiation showed no tumor masses (Fig. 2). Endocrine and immunological examinations revealed secondary hypopituitarism and impaired cellular and humoral immunity. During the next months patient carried out systemic chemotherapy with BCNU/etoposide/cisplatin and complete remission was achieved. The long-term clinical, neuroimaging (Fig. 3-4) and immunological (Fig. 5-7) findings corresponded with the stable course of the disease, lack of tumor recurrence, and tendency to recovery of im-

immune status. Clinical signs of neuroophthalmic (reduced visual acuity and bitemporal hemianopsia) and (Fig. 8) endocrine (hypopituitarism) impairment still persisted. Our patient was lost to follow-up five years after the tumor resection.

DISCUSSION

Germ cell tumors account for only 2-5% of all CNS malignancies and germinoma is the most frequent type in the brain. Previous findings suggest that males are affected more commonly than females, with an estimated ratio of 2:1 [3, 11, 21]. Approximately 95% of the primary brain germ cell neoplasms are found in the midline, in the pineal or suprasellar regions.

According to the literature, at the time of diagnosis about 5% to 10% of all germ cell tumors are found simultaneously in both regions, predominantly in patients with germinomas [10, 11, 28]. The clinical expression of these tumors is usually related to their location, size and speed of growth. Past and current studies demonstrate that the classic triad of symptoms of suprasellar germinomas includes DI, hypopituitarism and visual symptoms [3, 8, 17]. The most common visual symptoms are deficits in visual acuity, diplopia and bitemporal hemianopsia, dissociation of light and accommodation and paralysis of upward gaze [15, 18, 21].

Germinomas growing into the third ventricle may compress the hypothalamus, resulting in endocrine and immune dysfunction [3, 5, 9, 15]. Germ cell tumors in the pineal region most commonly present with hydrocephalus, visual symptoms (Parinaud's Syndrome), pyramidal tract signs and ataxia [29].

We suggest that our findings concerning patient's individual characteristics, past medical history and clinical presentation are similar to those described in the literature as a classic triad of germinoma-associated symptoms.

Numerous studies illustrate that the diagnosis of suprasellar and pineal germinomas is based on the clinical presentation, neuroimaging findings (CT/MRI), tumor biopsy, as well as additional specific endocrine and immunological tests [2, 17, 19, 20, 21]. Neuroradiologically, most of these lesions are well circumscribed and display a homogeneous contrast enhancement [14, 16]. Our CT findings (Fig. 1) are in correspondence with these previous results.

According to the literature, the endocrine examinations most commonly report findings of DI, hypogonadism, hypothyroidism, secondary adrenal insufficiency, hyperprolactinemia and pituitary dysfunction [3, 8, 15, 21]. The routine and specific blood and urine studies in our case show also evidence of DI and secondary hypopituitarism. Past immunological investigations detect different

anomalies in cellular and humoral immunity [9]. Especially, it is clear that the compression or lesion of the hypothalamic-pituitary region may abrogate functional activity of macrophages, lymphocytes and natural killer cells, as well as cause total and T-helper lymphopenia [5].

Patient's immunological monitoring (Fig.5) demonstrates initially impairment of cellular and humoral immunity corresponding to tumor location and therapeutic procedures and later on tendency for recovery of immune status after surgery, radio- and chemotherapy. We find our immunological study to confirm the previous reports both suggesting the immunoregulatory function of hypothalamus and the role of iatrogenic (post treatment) immunosuppression [9, 12, 13, 22].

Taking in consideration the results from the clinical, CT, histological, immunological and lab examinations we diagnose a germinoma with synchronous lesions in both suprasellar and pineal regions. In accordance with the literature, our differential diagnosis includes pituitary adenomas, craniopharyngiomas, true pineal tumors, gliomas, meningeal tumors, metastases, other germ cell tumors and vascular anomalies.

The overall treatment of germinomas involves radiation, chemotherapy, surgery, and management of endocrinopathy [2, 17, 21]. Depending on the location of the tumor, surgery may be used for both diagnostic biopsy and resection [10, 23]. Although optimal dosing and extent of radiation remains controversial, the previous reports suggest that germinomas respond well to irradiation [4, 16, 20, 25]. Because of their location germ cell tumors are often treated with chemotherapy [1, 7, 27].

Recent evidence exist that the best survival and least long-term morbidity is achieved with a combination of both chemotherapy and radiation [1, 6, 7]. The mortality rate is minimal for germinomas, with an estimated survival rate of 75-95% at both 5 and 10 years, depending on varying treatment protocols [4, 7, 24, 26]. Although some differences in the irradiation and drug regime, the good response that we achieved with the combination of surgery, radio- and chemotherapy (etoposide/cisplatin) corresponds to these previous findings.

In conclusion, we consider the synchronous suprasellar and pineal germinomas a rare occurrence with clinical expression specific for both regions. The differential diagnosis is based on the typical clinical features, contrast-enhanced CT/MRI, specific endocrine and lab tests, as well as histological verification.

Although their good prognosis, the review of the literature and our own notices suggest that they still present a diagnostic and therapeutic challenge. Therefore, the clinical, neuroimaging, and immunological follow-up may significantly improve their management and prognosis.

Fig. 1-2. Initial CT scans.

Fig. 3-4. CT scans after surgery, radio- and chemotherapy.

Initial contrast-enhanced CT scans demonstrate hyperdense tumor mass in the suprasellar and pineal regions. CT follow-up shows no evidence of tumor mass after surgery, radio- and chemotherapy, progression of hydrocephalus

(enlargement of third ventricle) after radio- and chemotherapy and tendency to its reduction (most evident in the temporal horns of lateral ventricles) several months later.

Fig. 5. Immunological monitoring of Leu, Ly and T-Ly.

Fig. 6. Immunological monitoring of %Ly, %T-Ly and macrophage activity.

Fig. 7. Immunological monitoring of T-h/T-s, SDH and β -GPDH.

Immunological monitoring shows initial impairment of cellular and humoral immunity, temporary progression of

immune deficit after radio- and chemotherapy, and tendency to recovery several months later.

Fig. 8. Patient's kinetic perimetry.

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