ANAPLASTIC ASTROCYTOMA POST RADIOTHERAPY OF PINEAL GERMINOMA

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Intracranial germ cell tumors (GCTs), especially pineal tumors have attracted the special attention of neuropathologists and neurosurgeons because of their unique growth sites, characteristic subtypes with different histology, and high incidence in Japan and other Asian countries[1]. They are usually arise in midline structures, including the pineal or suprasellar regions, more commonly seen in pediatric patients than in adults[2,3]. Radiosurgery is increasingly being used to treat pineal region tumors, either as an additional therapy after conventional treatments, the potential for late effects makes the treatment controversial[2].

Radiation-induced intracranial neoplasms are uncommon but well described and include gliomas, meningiomas, and sarcomas[4-6].

Germinoma developing an anaplastic astrocytoma is a rare event of radiation-induced intracranial tumors.

CASE

A 46-year-old female, at the age of 38 yr, presented signs of intracranial hypertension, and visual disturbances. MRI-imaging showed a pineal tumor (Fig 1A). The intraoperative smear showed round cells with vesicular and prominent nucleoli and clear, glycogen-rich cytoplasm (Fig 1B). The tumor was excised and the histopathology showed a germinoma (Fig 1C), and was

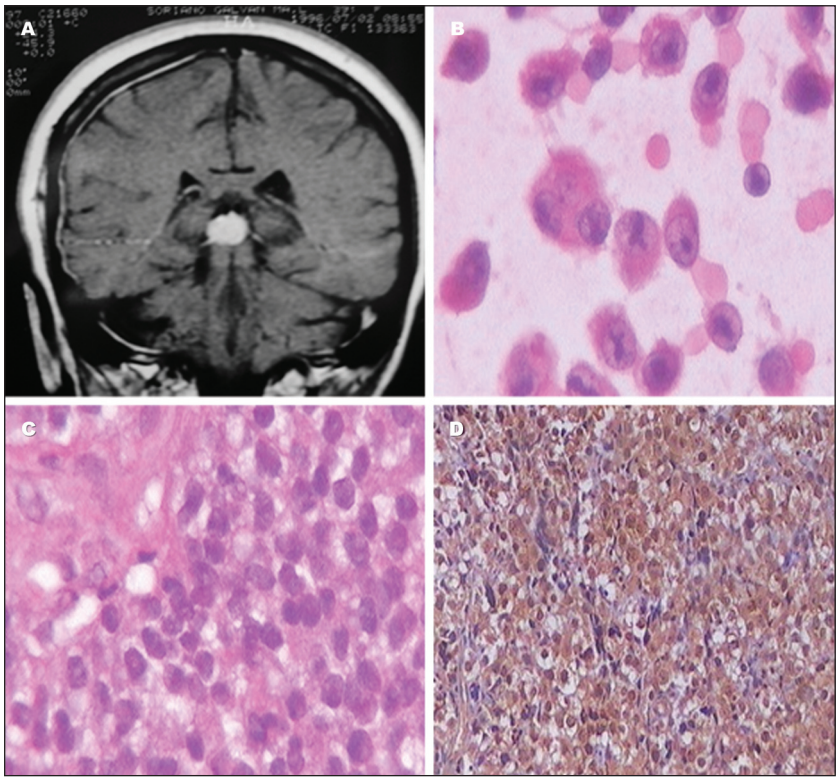

Fig 1. [A] The first MRI-imaging demonstrated an hyperintense on T1 and T2, 20 x 22 mm round contrast enhancing mass in the pineal region with anterior extension along the cistern of the velum interpositum, compressing on the posterior third ventricle. [B] Intraoperative pap smear showed a homogenous cells with a prominent nucleoli (H&E x 400). [C] The germinal tumor showed a homogeneous cell population with prominent nucleoli and scarce of lymphoid cells (H&E x 400). [D] Immunohistochemistry for fosphatase alcalin placentary (original magnification x 400)

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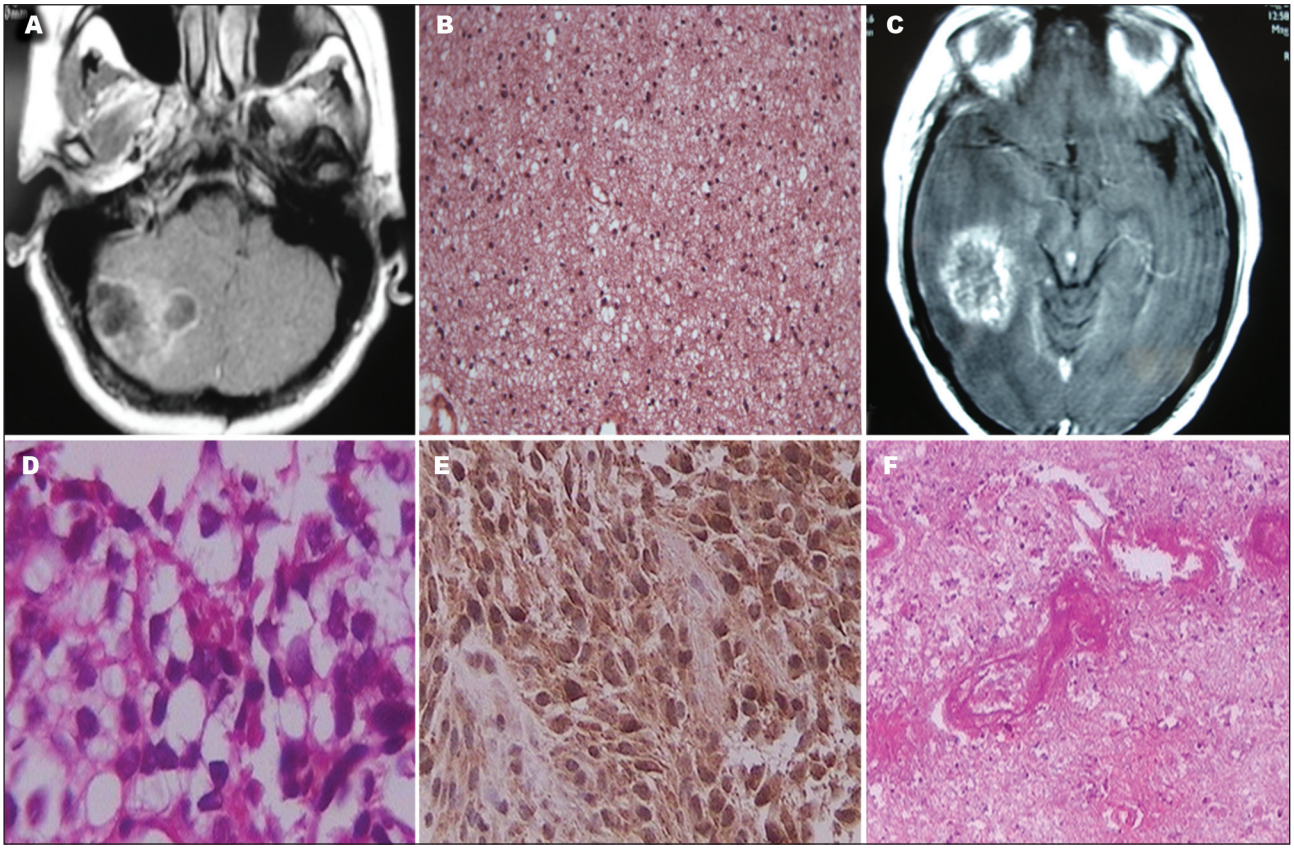

Fig 2. [A] The second coronal MRI-scan showed a mass consist of cystic and solid components in the right cerebellar hemisphere, showing a well demarcated, slightly nonhomogeneous cystic lesion with an enhancing mural nodule. [B] Histological features showed astrocytes proliferation with fibrillary background, no atypias and pleomorsphisms were observed (H&E x 400). [C] Third tumor, coronal MRI-imaging showed in the right temporo-parietal enhancement an irregular thick kinglike wall with central hypointensity with radio necrosis changes. [D] Histological findings showed eosinophilic, pleomorphic and anaplastic cells with big and nucleolus and with mitosis features (H&E x 400). [E] GFAP positive reaction (IHQ x 400). [F] Adjacent normal brain tissues of the third tumor showed radio necrosis signs (H&E x 200).

Table. Antibodies used and results.

Antibody used	Source clone	Dilution	Pineal tumor	Cerebellar tumor	Temporal tumor
Glial acidic fibrilar protein	DAKO	1:100	negative	positive	positive
Sinaptophysin	DAKO	1:100	negative	negative	negative
PCNA	DAKO	1.100	16%	27%	59%
Ki-67(MIB-1)	KAKO	1:100	3%	6.4%	43%
P-53	DAKO	1:100	negative	negative	positive
Fosphatase alcalin placentary	DAKO	1:100	positive	negative	negative
Neuron specific enolase	DAKO	1:100	Negative	negative	Negative
Beta chorionic gonadotropin	DAKO	1:100	negative	negative	negative
Tubulin	DAKO	1;100	negative	negative	negative

DAKO cytomation Carpintery Ca.

immunopositive to fosphatase alcalin placentary (FAP), and glial acidic fibrillary protein (GAFP) was negative (Fig 1D). She had received radiation therapy with 50Gy.

Five years later, she presented headaches, memory loss, depression and complex partial seizures. MRI-imaging disclosed ring-like enhanced mass lesion in the left cerebellar lobe (Fig 2A). Tumor biopsy was performed through a suboccipital approach. The tumor was partially excised (80%) The histological diagnosis showed a grade I fibrillary astrocytoma (Fig 2B). It was GFAP+, P53– and MIB-1Li of 6.4%. The patient received post-op-

erative chemotherapy and radiotherapy (RT), at total dose of 40Gy. She received a 6-week course of chemotherapy (lovustine, CCNU). During the next 3 years remained clinically and radiographically stable. However, she presented seizure activity, and imaging studies were consistent with tumor recurrence. She showed frontal cephalea, psychotic depression, amaurosis, right hemiplegia, and cerebellum syndrome. MRI-images disclosed enhanced mass lesion in the right temporal lobe corresponding to the previous irradiated field (Fig 2C), Right temporal lobectomy were performed. Histological showed astrocytoma grade III (Fig 2D), was GAFP+ (Fig 2E), P53+ and MIB-1Li was 43% (Table), with features of radiation effects (Fig 2F). The postoperative course was eventfully and died. An autopsy was not performed.

DISCUSSION

Total removal of pineal tumors is the therapy of choice[2]. Subtotal resection, atypical histological features, and high cell proliferation rates correlate with recurrence[1-3]. Radiotherapy has shown to be effective and has been given for pituitary tumor, astrocytoma, pinealoma, craniopharyngioma, glioblastoma and metastasic carcinoma[2].

The clinical features and long-term outcome with delayed cerebral radiation necrosis (DCRN) are described[4,5], produces a distinctive clinical picture, and remains a poorly recognized complication of cranial irradiation[6].

Cerebral vascular disease has been reported as a long-term complication of cranial radiotherapy too[7]. The mean latency to onset of the first neurological symptoms are 22 months (range 6–40 months), and mean duration of follow-up is 86 months (range 60–126). Patients with germinona may die after radiotherapy at a mean of 84 months (range 62–98[3,4]).

The differentiation of radiation-induced gliomas from radionecrosis of the brain is also discussed[8]. The period of latency before tumor occurrence ranges from 5 to 22 years with a mean of 10 years. The precise clinical features that correlate irradiation and oncogenesis are not completely defined, but some authors have suggested that tumors are radiation-induced when they are histologically different from the treated ones, and arise in greater frequency in irradiated patients than among normal, and tend to occur in younger people with an unusual aggressiveness[7].

The criteria for radiation-induced tumor have been established by Cahan et al[8]. A tumor location within irradiated area, no evidence of tumor prior to radiotherapy, a long latency period between radiation and tumor occurrence, and histological verification of the primary tumor must be pathologically different from the primary tumor and present at the time of irradiation and there must be no genetic predisposition for second tumor[8].

The morphological and immunohistochemical features of intracranial germ cell tumors are very similar to those of gonadal germ cell tumors[1-3]. However, the immunohistochemistry remains still very helpful in differential diagnosis[1].

Henson JW et al.[9], reported that some primary human astrocytomas increase expression of p53 and p21 and decrease proliferation in response to RT. However, the small size of the series argues for further studies of radiation-induced molecular changes in primary human astrocytoma tissue.

In summary, we present a 46 years-old female who received radiotherapy of pineal germinoma. 5 year later she presented a second tumor an astrocytoma grade I, in cerebellum, received radiotherapy and 3 years later, presented a third different tumor, an anaplastic astrocytoma in the temporal lobe, associated to cerebral radio necrosis. Although radiation-induced neoplasia followed by radiotherapy is diagnosed.

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