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Oncology

PINEAL PARENCHYMAL TUMOR OF INTERMEDIATE DIFFERENTIATION: CASE REPORT AND LITERATURE REVIEW

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ABSTRACT **Summary:** Pineal parenchymal tumors of intermediate differentiation (PPTID) are extremely rare malignancies, only limited data are available regarding their pathological behavior, pineal parenchymal tumors (PPT) account for less than 1% of all primary central nervous system neoplasms, PPT of grade II and III are grouped under name of PPTID, ranging between pinealocytoma (grade I) and pinealoblastoma (grade IV), we report the case of a 32 years old young woman treated in the radiation oncology department of Mohammed VI university hospital of Marrakech for a PPTID, the disease was revealed by an intracranial hypertension syndrome with vision acuity loss and Argyll Robertson syndrome, imaging shows no dissemination, the patient underwent first an endoscopic third ventriculostomy and then a stereotaxic biopsy, treatment consisted on 54 Gy local external beam radiation therapy with partial response, after a follow-up of 7 months the patient is still in remission.

KEYWORDS : Pineal parenchymal tumor-Pineal parenchymal tumor of intermediate differentiation-radiotherapy-treatment

Background

The pineal, an endocrine gland of 6 mm, Producing melatonin, is located behind and beneath the stria medullaris, between the 2 thalami, in dorsal to the superior colliculus.

Pineal parenchymal tumors (PPT) account for less than 1% of central nervous system malignancies,[1] pineal parenchymal tumors of intermediate differentiation (PPTID) are extremely rare entity representing the grade II and III of PPT. [2]

If gross tumor resection is considered, for many authors, the standard of care in PPT, there is no consensus regarding adjuvant therapies.

Case presentation

We report the case of a 32 years old woman presenting with Argill-Robertson syndrome with profound and homogenous loss of visual acuity of the right eye, moderate decrease of visual acuity of the left eye, without ocular paralysis nor sleep troubles nor other neurological deficit.

Investigation

Magnetic resonance imaging (MRI) showed a T1-hyposignal, T2-hypersignal heterogeneous lesion of the pineal region with tri-ventricular hydrocephalus (Figure 1,2).

The young woman underwent an endoscopic third ventriculostomy intervention followed 2 months later (after regression of intra-cranial hypertension related symptoms) by a stereotaxic biopsy.

Germ cell tumors markers were negative.

Medullary MRI showed no secondary lesion.

Histological exam showed a malignant small round cell proliferation (Figure 3;4)

Immunohistochemistry showed an intense and diffuse expression of synaptophysine (Figure 5) and NSE (Figure 6), with 10% of cells expressing Ki67 Antigen (Figure 7).

Differential diagnosis

As germ cell tumors are the most frequent neoplasms in pineal region, it was necessary to eliminate this diagnosis first, germ cell tumor markers were negative and immunochemistry concluded to a pineal parenchymal tumor of intermediate differentiation.

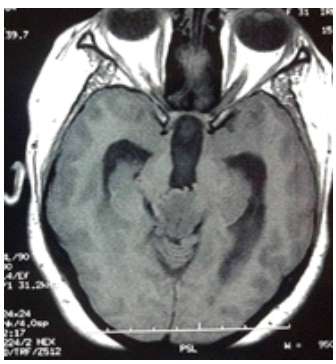

Figure 1: T1 magnetic resonance imaging sequence showing a hypo-signal lesion of 2x1,5 cm of the pineal region with triventricular hydrocephalus.

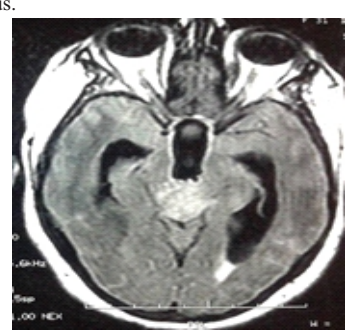

Figure 2: T2 flair MRI sequence showing a heterogeneously hyper-signal lesion of pineal region with moderate peri-tumoral swelling.

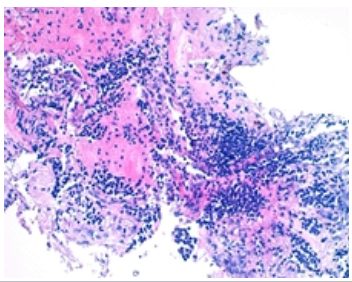

Figure 3: Small round cell proliferation (Hematoxylin and eosin stain; x20)

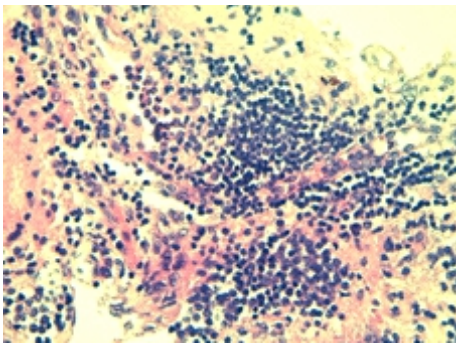

Figure 4: Small round cell proliferation (Hematoxylin and eosin stain; x20)

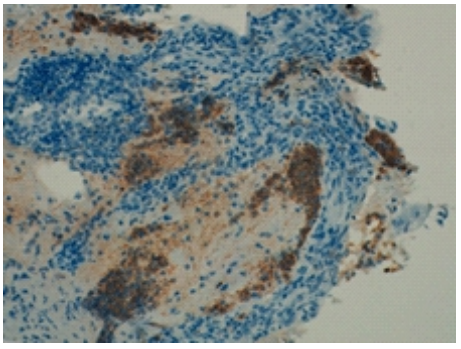

Figure 5: Positive immune-staining for synaptophysine antibody (x20)

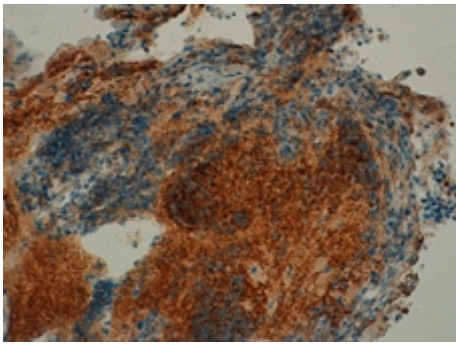

Figure 6: Positive immune-staining for NSE antibody (x20)

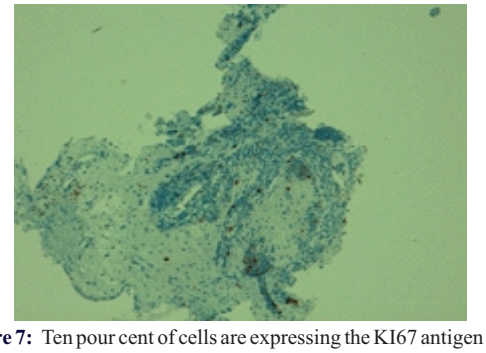

Figure 7: Ten pour cent of cells are expressing the KI67 antigen (x10)

Treatment

The young woman had received a 3D conformal radiotherapy of 54 Gy in 30 fractions.

Post-radiation MRI showed a partial response, with good clinical response, partial recuperation of visual acuity of the left eye without improvement of the right eye visual acuity

After a follow-up of 7 months, MRI shows no sign of recurrence, the young woman is still in remission.

Discussion

Pineal parenchymal tumors are malignancies arising from pineocytes in the region of the pineal gland, representing less than 1% of central nervous system cancers,[1] it occupies the second range of pineal region tumors after germinal neoplasms. [3]

The 2007 World Health Organization classification of tumors of the central nervous system categorizes PPT as pinealocytoma (grade I), pineal parenchymal tumors of intermediate differentiation (grade II or grade III) and pinealoblastoma (grade IV). [2]

PPTID generally occurs in adults, with a sharp female predominance. [5]

MRI even if not specific usually shows a T1-hypointense, T2-isointense, heterogeneously contrast-enhancing partially cystic mass in the pineal region, spinal screening magnetic imaging and cerebro-spinal-fluid (CSF) analysis are systemic to detect eventual spinal metastasis or CSF spreading as the risk of leptomeningeal recurrence is more than 10%, [5] PPTID may be with differential diagnosis with pinealoblastoma by its locally invasive character.

Pinealocytoma are considered to be locally-limited malignancies with good prognosis and limited invasive potential, the prognosis of PPTID seems to be largely better than pinealoblastoma, Lutterbach and al [6] reported a median survival of 165 months and 77 months for PPTID and pinealoblastoma respectively (p=0,001).

The largest primary report published in 2000 including 76 cases of PPT in 12 European centers treated between 1972 and 1997, [7] demonstrate a 5-year survival of 91%, 74%, 39% and 10% for grades I-IV PPT respectively, this study showed a good outcome correlated with age above 20 years, tumor diameter less than 25 mm and low grade histology, multivariate analysis confirmed histology and tumor volume to be independent prognosis factors.

Lutterbach and al, [6] stated that extend, differentiation, age and residual tumor size were independent prognosis factors of overall survival in the 101 patients with malignant PPTIDs and pinealoblastomas.

The study of Villa and al [8] published in 2012 including 35 cases of PPT, showed that age younger than 36 years and presence of metastasis at diagnosis were unfavorable prognosis factors.

Pinealoblastomas could be compared to medulloblastomas and are managed with aggressive multimodal approach combining surgery, radiotherapy and chemotherapy, because of their highly malignant biological behavior [10,11], for pinealocytomas complete surgical resection could provide a chance of cure [8,12]. Concerning PPTID, the limited number of published cases explain the reason there is no consensus regarding treatment.

In the study of Motiei and al, [9] including 48 cases of pineal region tumors (germinal, glioblastomas and PPT) comparing gross tumor resection to stereotaxic biopsy, authors concluded that although gross total resection is the standard of care of pineal region tumors, stereotaxic biopsy with adjuvant radiotherapy (with or without chemotherapy) is a viable option.

In a recent analysis of 29 publications (129 cases of PPTID), [5] median age was 33 years, The median progression free survival and overall survival were 5,17 and 14 years respectively, surgery was the commonest treatment, adjuvant radiotherapy was performed in third cases, and adjuvant chemotherapy in 26%, indications to adjuvant treatment varied widely depending on local practices, among patients who had reccurence 62,5% experienced spinal or lepto-meningeal recurrence while 37,5% had local recurrence, univariate analysis found a better survival rate in patients who received adjuvant radiation (252 months versus 168, p=0,009) while age, surgery extension and adjuvant chemotherapy had no significant impact on overall survival, authors recommend radiotherapy in all patients with less than a gross total resection, local radiotherapy should be preferred over cranio-spinal radiation considering its toxicity, cranio-spinal radiation is recommended in patients with medullary dissemination.

The study of Fauchon and al, [10] including 74 patients with PPT, revealed extend of radiotherapy has no clear influence on survival.

The study of Schild and al, [13] of 30 patients with PPTs, showed an improved 3-year survival in patients who underwent radiotherapy with doses exceeding 50 Gy compared to those with lower radiotherapy doses (94% VS 56%), suggesting a better survival with dose-escalated radiotherapy.

The study of Das and al, [14] analyzing retrospectively outcomes in 5 patients with local PPTID for whom gross total resection was impossible, treated with post-operative local external beam radiotherapy (54 Gy in 30 fractions), 4 patients had partial response and one had stable disease, no patient developed recurrence after 21 months of follow up, all patients were alive at the end of observation period.

The recently published study of Park an al, [15] including 9 cases of PPTs (PB and PPTID) treated between 1997 and 2014 with stereotaxic radio-surgery, 3 patients had complete response and 6 had partial one, after a mean follow-up of 78 months, one patient presented with remote CSF seeding metastasis 7 years after treatment.

It seems to be justified and logical to set chemotherapy as adjuvant treatment in patients with CSF dissemination or in case of recurrent disease, the association platinium, etoposide may be considered, as in medulloblastoma. [5]

Learning points

Pineal parenchymal tumors occupy the second range of pineal region malignancies after germinal neoplasms.

Pineal parenchymal tumors of intermediate differentiation represent grade II and III of pineal parenchymal tumors.

Surgical resection plus adjuvant radiotherapy is the most often adopted strategy.

Stereotaxic radiosurgery has shown promising outcomes and could be an alternative to surgical resection.

Adjuvant chemotherapy and cranio-spinal radiotherapy are defended in disseminated cases.

Footnotes

Competing interests: none.
Patient consent: obtained.

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