Late dissemination via cerebrospinal fluid of papillary tumor of the pineal region: a case report and literature review

Elżbieta Nowicka1, Barbara Bobek-Billewicz2, Janusz Szymański3, Rafał Tarnawski1

13rd Radiotherapy and Chemotherapy Department, Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, 2Department of Radiology, Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, 3Pathology Department, Poznan University of Medical Science, Poznan, Poland

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Abstract

Papillary tumor of the pineal region (PTPR) represents a recently described entity and was included in the 2007 World Health Organization (WHO) classification of central nervous system tumors. The biological and clinical behavior of PTPR is variable and may correspond to WHO grades II or III. Papillary tumor of the pineal region can show aggressive biological behavior with local relapses and dissemination via the cerebrospinal fluid. Several cases of PTPR with leptomeningeal seeding and multiple lesions or spinal metastasis have been reported. We present an unusual clinical history of papillary tumor of the pineal region with ventricular and spinal dissemination five years after primary surgical treatment.

Key words: papillary tumor of the pineal region, cerebrospinal fluid dissemination.

Introduction

Pineal tumors account for less than 1.0% of all intracranial tumors [2]. Papillary tumor of the pineal region (PTPR) was for the first time described in 2003 by Jouvet et al. [5]. Papillary tumor of the pineal region was included in the 2007 World Health Organization (WHO) classification of central nervous system tumors [8]. The diagnosis of this neoplasm is often difficult because of its similarity to other primary or secondary papillary lesions of the pineal region, including parenchymal pineal tumors, papillary ependymoma, papillary meningioma, choroid plexus papilloma and metastatic papillary carcinoma [2]. The cell of origin is thought to be specialized ependymocytes of the subcommissural organ [3]. The biological and clinical behavior of PTPR is variable and may correspond to WHO grades II or III, but there are no precise histological grading criteria defined [8,9]. Papillary tumor of the pineal region can show aggressive biological behavior with local relapses and dissemination via the cerebrospinal fluid. Several cases of PTPR with leptomeningeal seeding and multiple lesions or spinal metastasis have been reported [1,2,4,6,7,10,11]. The optimal therapeutic approach of PTPR has not been well defined [1].

We present an unusual clinical history of papillary tumor of the pineal region with ventricular and spinal dissemination five years after primary surgical treatment.

Communicating author

Elżbieta Nowicka, 3rd Radiotherapy and Chemotherapy Department, Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, 16 Wybrzeże Armii Krajowej St., 44-100 Gliwice, Poland, e-mail: enowicka@io.gliwice.pl
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Case report

A 62-year-old Caucasian man who was admitted to the Center of Oncology MCS Memorial Institute in April 2013 after neurosurgical intervention due to the tumor of the foramen magnum region. He had his first neurosurgical intervention in the Neurosurgery Department in 2007. The first neurological symptoms were headache, loss of memory, psychosomatic retardation and vertigo in 2007. The magnetic resonance (MR) showed signs of significant hydrocephalus due to well circumscribed 20 × 13 mm large tumor in the pineal region. The tumor showed high intensity in T1 weighted images as well hyperintensity in T2 weighted images (Fig. 1A-B).

The patient did not accept a contrast injection so examination was performed without intravenous contrast and the data concerning contrast enhancement are not available. The patient underwent the suboccipital craniotomy and the tumor was totally removed. Histological examination of this tumor (Fig. 2, Appendix 1) had revealed cellular epithelioid tumor with papillary areas which did not demonstrate sufficiently well formed pseudorosettes supporting the diagnosis of ependymoma. At this time (2007) due to lack of sufficient experience with PTPR, this tumor was classified as pineocytoma, grade II.

Craniospinal axis magnetic resonance imaging (MRI) scans were not recommended at that time. The patient did not receive any adjuvant therapy and was referred to regular MRI brain scans once a year. In October 2012, MRI revealed the pathological mass in the foramen magnum region which met the radiological criteria of meningioma, which was not seen in the MR scan performed after surgery in 2007 (Fig. 3A-B). At that time there was no tumor mass in the pineal region The suboccipital craniotomy, laminectomy and total tumor removal was performed in February 2013.

The pathologic examination of the operation specimen was performed in the Pathology Department of Poznań Medical University (Fig. 4, Appendix 2). The tumor was 14 × 9 mm large. The tumor was solid, infiltrative, white-gray in color. Microscopic evaluation did not confirm the expected meningioma diagnosis. Histological examination showed a subtly epithelial partly papillary morphology. The papillae were closely-packed and covered by layers of large polygonal columnar cells with oval nuclei, fine stippled chromatin, and a moderate amount of clear, vacuolated or pale eosinophilic cytoplasm. Mitosis, tumor necrosis or microvascular proliferation was lacking. Preliminary diagnosis was a papillary tumor of the pineal region. Immunohistochemical stains revealed diffuse

![Fig. 1. T1-WI without contrast enhancement demonstrates well-delineated, slightly hyper intense mass in the pineal region. The lateral ventricles are enlarged with surrounding low-intensity interstitial edema as well as marked widening of the third ventricle are seen. No other tumors were found. A) Axial, B) sagittal.](https://example.com/fig1.png)
positivity for neuronal specific enolase, vimentin, cytokeratin 18 and the lack of neurofilament protein. Positive reaction for synaptophysin was seen only in a few neoplastic cells, whereas the expression of chromogranin A was negative. The tumor tissue did not exhibit GFAP expression. Proliferation index (Ki67) by immunostaining for MIB-1 was estimated to be about 10%. (Fig. 5A-D). An extra comparative histological and immunohistochemical examination was done with the material from the first surgery in 2007. The primary tumor which was originally classified as pineocytoma WHO II, after subsequent comparative analysis presented the same morphology and immunohistological profile as the second tumor. Based on the clinical behavior of the tumor, histopathological and immunohistochemical analyses, the final pathological diagnosis was a papillary tumor of the pineal region (PTPR), grade III.

The patient was referred to an oncology consultation in the Center of Oncology in Gliwice in April 2013. He was in good performance and neurological status. Clinical examination did not reveal any variations. An independent review and reanalysis of post-operative tissue blocks from the first and the latter surgical intervention were performed in the Department of Tumor Pathology in the Center of Oncology in Gliwice. The pathological consultation of paraffin embedded tissue confirmed primary diagnosis of the papillary tumor of the pineal region.

The MRI data were reviewed by radiologists and extra MRI scans of the cereobspinal axis were done. The radiological examination revealed no tumor mass in the pineal region and total tumor resection of the foramen magnum region tumor (Fig. 6), but...
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Fig. 3. Sagittal T1-WI C+. A) Well-circumscribed, homogeneously enhancing intradural extramedullary mass with a broad dorsal dural attachment in the foramen magnum (at the craniovertebral junction) (2012). The tumor is not seen in the scan performed after surgery in 2007 (B).

Fig. 4. At 2013 histological examination showed a subtly epithelial partly papillary morphology. The papillae were closely-packed and covered by layers of large polygonal columnar cells with oval nuclei, fine stippled chromatin, and moderate amount of clear, vacuolated or pale eosinophilic cytoplasm (Lab. number 499969 A and B).

A few small contrast enhancing foci up to 7 mm in diameter in the subependymal region of frontal (anterior) horns and stem of lateral ventricles with radiological image of metastases were diagnosed (Fig. 7A-C). The dissemination in the spinal axis was excluded. The patient was referred to radiotherapy and the decision was made to perform the craniospinal irradiation. From 26.06.2013 to 29.07.2013 the patient was irradiated with tomotherapy. The conventional fractionation was used with 1.8 Gy/g per fraction to the total dose of 36 Gy/g. The treatment was completed with good general and neu-
Appendix 2. Metastatic tumor 499969

http://150.254.71.142/vf1.aspx?&mo=1&im=3874&-type=SlideIndex&sid=xr2ezi32vmjuwhr2tlwcrp&d=Vmp BeGFGeHWEjyWtVDi5O#/overlay/vectoroverlay

Fig. 5. Immunohistochemical stains revealed diffuse cytokeratin 18 positivity. The tumor tissue did not exhibit GFAP expression. Proliferation index (Ki67) by immunostaining for MIB-1 was estimated to be about 10%. Positive reaction for synaptophysin was seen only in a few neoplastic cells.
Discussion

Primary papillary tumor of the pineal region is a rare neoplasm. It was first described by Jouvet in 2003 and was finally included in WHO 2007 classification of tumors of the nervous system [2,8]. Only 72 cases have been described in the literature to date [10].

These rare tumors of the pineal region manifest in children and young adults (mean age 32 years) [4,11]. Histologically, papillary tumors of the pineal region are characterized by a papillary architecture and cellular epithelioid morphology. Crucial for differential diagnosis is specific immunohistochemical profile with strong reactivity to cytokeratin CK18, S-100, neuronal specific enolase (NSE), vimentin and focal or low glial fibrillary acidic protein (GFAP) [2,3,5,8,9]. The biological behavior of PTPR is variable and may correspond to WHO grades II or III [8]. Although there are more and more clinical data accumulated over last years on treatment modalities and outcomes, the treatment strategies are not well described. Surgical resection with subsequent local radiotherapy is current standard of care [8]. There are some data on chemotherapy use especially when local recurrence or spinal dissemination is diagnosed [1]. In the largest series of 44 patients with PTPR, the role of surgery, radiotherapy, and chemotherapy was analyzed by Fauchon et al. Median follow-up was 63.1 months. Median overall survival (OS) was not achieved. Median progression-free survival (PFS) was 58.1 months. Only gross total resection and younger age were associated with a longer OS, radiotherapy with chemotherapy having no significant impact. Progression-free survival was not influenced by gross total resection. Radiotherapy and chemotherapy had no significant effect. This retrospective series confirms the high risk of recurrence in PTPR: 58% at five years and 70% at six years [1]. Three out of 44 reported patients had the evidence of spinal cord seeding; one initially and the remaining while recurrence [1].

PTPR might display local recurrences and CSF dissemination despite surgical resection and radiotherapy [1,3,6]. Due to their localization the PTPR cells may spread via the cerebrospinal fluid [4,6]. In the series of 31 patients analyzed by Fèvre-Montagne et al., the majority experienced recurrences: 5-year overall survival and progression-free survival were 73% and 27%, respectively [3].

![Fig. 6. Sagittal T1-WI C+ revealed no tumor mass in the pineal region and total tumor resection of the foramen magnum region tumor in 2013.](image-url)
Fig. 7. Axial T1-WI C+ FS shows contrast enhancing subependymal nodules in the frontal horn of the left lateral ventricle before (A) and 5 months after RT (B); in the frontal horn of the right lateral ventricle before RT (C) and 5 months after RT (D). The small enhancing subependymal nodules in the lateral ventricles remain essentially unchanged on the post treatment MRI scan performed 6 and 10 months following completion of radiotherapy.

Another clinical report of leptomeningeal seeding by Kim et al. is the case of a 39-year-old woman who presented a history of headache and decreased visual acuity. Magnetic resonance imaging showed solid and cystic, contrast enhancing mass at the pineal region with associated ventriculomegaly. Smaller and contrast enhancing nodular lesions were also found at the pituitary stalk and bilateral internal acoustic canals. After endoscopic ventriculostomy the partial resection was performed. The pathological examination of the specimen revealed the features of PTPR. Despite the radiotherapy of the lesions through
gamma knife radiosurgery and a decrease in size of the primary lesions on MRI six months afterwards, new enhancing lesions occurred. The case presented is a proof that PTPR can disseminate to other sites distant from the original lesion [6].

We report the case of a 61-year-old man who was first operated in 2007 with the initial pathological diagnosis of pineocytoma. During the follow-up period the MRI scans showed the tumor in the foramen magnum region resembling meningioma, which was not seen in the MR scan performed after surgery in 2007. After surgery and histopathology examination of the specimen, the final diagnosis established in 2013 was PTPR. After re-examination of the tissue blocks from the first operation, the same morphology was presented. The immunohistochemical reactivity confirmed the diagnosis of PTPR. Magnetic resonance imaging showed the dissemination to the subependymal region of frontal (anterior) horns and stem of lateral ventricles. Our clinical data as well as already published series of PTPR patients indicate that the pattern of cerebrospinal fluid dissemination is possible. Concurring with other authors we strongly encourage the primary cerebrospinal axis MR imaging, after the PTPR is diagnosed [4,10]. Obvious cerebrospinal fluid dissemination in our patient led to a decision of craniospinal irradiation in order to treat visible dissemination in the brain and to prevent spinal seeding. The radiotherapy plan was similar to our protocol in patients with PNET or medulloblastoma. In a report of Fauchon et al., the radiotherapy to neuraxis was also performed in patients with craniospinal dissemination [1]. At the moment the follow-up is very short so we should wait for the outcome.

Papillary tumors of the pineal region are rare tumors with a strong propensity for local recurrences and which may disseminate via the craniospinal fluid. The clinical data on behavior of those tumors should still be followed and accumulated in a prospective, multi-center manner to enable the evaluation of the same diagnostic and treatment guideline consensus. What is important now from a practical point of view is the need for serial radiological examination of the entire cerebrospinal axis while the PTPR is diagnosed. It is not clear if cerebrospinal irradiation should be considered during the initial adjuvant therapy of PTPR.

Disclosure

Authors report no conflict of interest.

References