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Case Report

Pituitary Atypical Teratoid Rhabdoid Tumor in a Patient with MEN-1 Syndrome and Prolactinoma: A Case Report

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Abstract: Atypical teratoid/rhabdoid tumor (AT/RT) is a rare, aggressive central nervous system (CNS) neoplasm, typically diagnosed in children, with fewer than 100 adult cases reported. Pituitary prolactinomas, more common in adults, have been rarely associated with AT/RT, particularly in the context of multiple endocrine neoplasia type 1 (MEN-1) syndrome. We present a 38-year-old female with MEN-1 syndrome, recurrent pituitary prolactinoma, and AT/RT. She presented with altered mental status, headache, and seizure-like activity. CT imaging revealed a residual invasive pituitary tumor with significant hemorrhaging. Post-operative pathology confirmed the presence of both a pituitary prolactinoma and AT/RT. Molecular analysis of the AT/RT demonstrated a loss of INI-1 and a homozygous deletion of CDKN2A/2B. The patient was re-admitted a month later with signs of aggressive tumor recurrence and transitioned to hospice care. This case is one of only two documented instances of concurrent pituitary prolactinoma and AT/RT, and it is further complicated by the patient's MEN-1 syndrome. This report highlights the rare occurrence of AT/RT in adults and its potential association with prior radiation therapy for pituitary adenomas, raising questions about the impact of MEN-1 syndrome on AT/RT pathogenesis.

Keywords: MEN 1; prolactinoma; atypical teratoid/rhabdoid tumor

1. Introduction

Atypical teratoid/rhabdoid tumor (AT/RT) is a rare and highly aggressive central nervous system (CNS) neoplasm, predominantly diagnosed in pediatric patients. Fewer than 100 adult cases have been reported. In contrast, pituitary prolactinomas are more prevalent in adult populations, with an estimated annual incidence of 10–30 cases per 100,000 individuals. Although multiple endocrine neoplasia type 1 (MEN-1) syndrome is commonly associated with pituitary adenomas, there have been limited reports of AT/RT occurring concurrently with this syndrome. This case presents a 38-year-old patient with a history of MEN-1 syndrome, diagnosed with both recurrent pituitary prolactinoma and AT/RT. This case is exceptionally rare, as it is one of the only two documented instances of these two tumors occurring together in a single patient, and is further complicated by the rarity of AT/RT in adults.

2. Case Presentation

We present a 38-year-old female with a known history of MEN-1 syndrome and recurrent pituitary prolactinoma who was admitted to our facility in April 2024 due to altered mental status, headache, and seizure-like activity.

A CT scan at the time of presentation revealed a residual invasive macroadenoma predominantly affecting the right side of the sella turcica. The tumor extended into the right middle cranial fossa and involved the right

temporal lobe. Additionally, the scan revealed large intraparenchymal hemorrhages, with supra- and infratentorial intraventricular hemorrhage and dilation of the right lateral ventricle. The patient's family reported episodes of absence-like seizures over the preceding months.

The patient was promptly evaluated by neurosurgery and underwent resection of the pituitary mass, along with evacuation of the intraventricular hemorrhage. Initial pathology indicated a poorly differentiated neoplasm with high mitotic activity. Post-operatively, the patient was admitted to the neurosurgical intensive care unit, where an external ventricular drain was placed. Post-operative MRI demonstrated typical post-surgical changes without signs of tumor recurrence. The patient recovered and was discharged to an acute rehabilitation facility.

Final pathology, reported after discharge, confirmed the diagnosis of AT/RT. Two distinct tumors were identified: the first was the residual pituitary prolactinoma, with PIT1-positive tumor cells expressing prolactin. The second tumor was submitted to the National Institutes of Health (NIH) for methylation analysis, which revealed a high-confidence match to AT/RT, characterized by the loss of INI-1. Foundation-One testing revealed a homozygous deletion of CDKN2A/2B.

Unfortunately, the patient was readmitted one month later with generalized weakness and lethargy. A CT scan at an outside hospital showed concerning signs of AT/RT recurrence. Given the aggressive recurrence and poor prognosis, the decision was made to transition the patient to home hospice care. She passed away about 1 week later, approximately 2 months after the initial diagnosis.

3. Past Medical History

The patient's medical history is significant for MEN-1, which was also present in her mother, 2 maternal aunts and her maternal grandmother. In 2004, at age 17, she presented with amenorrhea and was diagnosed with a prolactin-secreting pituitary macroadenoma. Surgical debulking was performed, followed by treatment with cabergoline. In 2011, the tumor recurred, with MRI revealing a highly irregular pituitary mass measuring 3.8 × 5.3 × 3.4 cm, which extended into the bilateral cavernous sinuses and the right optic canal. Surgical resection was performed, followed by adjuvant radiation therapy.

The patient was lost to follow-up but presented again in 2013 with a significantly enlarged pituitary mass measuring 5.3 × 5.8 × 4.7 cm, which extended into the right subfrontal region, right middle cranial fossa, and bilateral cavernous sinuses. Her prolactin level was markedly elevated at 7550 ng/mL (ref range: 2.8–29.2 ng/mL). A subtotal resection was performed, and she was discharged on cabergoline. She later completed a course of external beam radiation therapy (XRT), finishing in August 2013, with a final dose of 52.2 Gy.

Between 2013 and 2021, the patient developed panhypopituitarism with central adrenal insufficiency, which was managed with hydrocortisone, and central hypothyroidism, managed with levothyroxine. Her case was further complicated by parathyroid hyperplasia, which required a three-gland parathyroidectomy in November 2003 and later a total parathyroidectomy with reimplantation of the right upper parathyroid into the left pectoralis muscle in April 2018.

Due to insurance issues, the patient was again lost to follow-up until her presentation in April 2024, which ultimately led to the diagnosis of AT/RT.

4. Discussion

According to the World Health Organization (WHO), AT/RT is diagnosed based on the presence of a poorly differentiated neoplasm with inactivation of SMARCB1 (INI1) or, rarely, SMARCA4 (BRG1) seen through immunohistochemistry or fluorescence in situ hybridization [1–3]. Specific molecular markers and genetic alterations are important in further classifying and identifying different types of AT/RT [3]. Sellar region ATRTs in adults show epigenetic similarities with pediatric ATRTs of the ATRT-MYC subgroup and have different patterns of INI1 alterations and histology showing unique hemangiopericytoma-like stag-horn vasculature [4,5]. While AT/RT tumors frequently exhibit rhabdoid morphology, these features are not specific or sensitive for AT/RT, as other CNS tumors, including epithelioid glioblastoma, meningiomas, metastatic carcinomas, chordomas, and sarcomas, can also display rhabdoid features [6].

AT/RT is the most common malignant brain tumor in children younger than 6 months, but extremely rare in the adult population, with approximately 100 reported cases [6–8]. In the pediatric population, tumor location is most commonly in the posterior fossa, and median survival is between 6 and 18 months [3,9]. In adults, median survival is around 15 months but varies significantly, with 22.9% of 5-year survival without evidence of disease [8]. While some patients die months after diagnosis, those who respond to treatment live for many years with no incidences of recurrence. The longest survival time documented is 17 years [6]. Contrary to the pediatric population, the most

common location of adult AT/RT is supratentorial [9]. Location of tumor and type of treatment (radiotherapy, chemotherapy, surgical resection) were important factors associated with patient outcomes.

The mean age of diagnosis is 38–44 years, with most patients being female (70–90%) [6,9]. The most common presenting symptoms include headache, visual disturbances, cranial nerve deficits, altered consciousness, and seizures [6]. Most tumors are intracranial, with the supratentorial region, particularly the sellar region, being the most affected. AT/RTs in the sellar region are associated with significantly worse overall survival compared to tumors in other locations. Tumors involving the brain hemispheres showed the best outcome with a median overall survival of 33 months, followed by tumors of the posterior fossa, spinal region, pineal region, and lastly sellar region (16 months) [7].

Different treatment options include a combination of surgical resection, radiotherapy, and chemotherapy. Survival was significantly improved in patients who received combined chemo-radiotherapy compared to those who received radiotherapy alone or no adjuvant therapy [6,9,10]. Surgical intervention combined with chemo-radiotherapy had a significant impact on survival compared to surgery alone or surgery with radiotherapy [6]. The location of the tumor influences the choice of surgical intervention. Over half of patients with AT/RT in the brain hemispheres received gross total resection, compared to only 15% of patients with sellar tumors [7]. Local invasiveness, frequently of vascular structures may explain the low rate of gross total resection in sellar tumors. However, when comparing all patients who received gross total resection, incomplete resection, and biopsy, no significant difference was found [6,10].

To our knowledge, there is only one other case report of a patient with a history of prolactinoma who later developed AT/RT [11]. In this case, diagnosis of prolactinoma also occurred years before diagnosis of AT/RT. Similar to our case, tumor location was intrasellar with local invasion. Neither patient had metastasis to other areas of the body, which has been seen in some cases of AT/RT [8]. This patient received radiotherapy following transsphenoidal removal of lesion compared to surgical resection alone for our patient. However, our patient had received prior radiation for treatment of prolactinoma. Another patient with AT/RT who subsequently developed pituitary apoplexy also showed elevated levels of prolactin, although without evidence of prior prolactinoma [12]. In all 3 cases prognosis was very poor with survival following initial admission <3 months. Several reports have explored the co-occurrence of pituitary prolactinoma and other sellar tumors, such as meningiomas, gangliocytomas, or fibrosarcomas. Prolactin receptors have also been found in several tumors of the CNS, including meningiomas, schwannomas, astrocytomas, and non-CNS tumors, including ovarian and endometrial carcinoma [13–15]. Elevated prolactin levels have been shown to promote cell proliferation, increase tumor metastasis, and even reduce sensitivity of cells to chemotherapy in endometrial carcinoma [14]. Possible mechanisms include transdifferentiation from neoplastic cells of the pituitary adenoma or prolactin-mediated tumorigenesis. In our case, the patient's prolactin levels were significantly elevated, which may have influenced tumor behavior.

Interestingly, prior reports have also investigated a potential connection between AT/RT and radiation exposure from the treatment of unrelated neurologic malignancies. Recent literature has documented five cases of presumed radiation-induced AT/RT tumors in adults [16]. Four of these cases followed radiation therapy for non-CNS tumors, including childhood leukemia, soft tissue sarcoma, and craniopharyngioma [16–19]. To our knowledge, this is the first reported case in which a prolactinoma was the primary tumor, and the second case involving a sellar mass. While all previous reports indicated gene mutations specific to radiation-induced DNA damage [16], no such markers were found in our case. This suggests that the AT/RT in this patient may have resulted from radiation, although it may also be linked to her history of MEN-1 syndrome.

5. Conclusions

AT/RT is an aggressive CNS tumor, rarely seen in adults, but with documented occurrence following radiation treatment of non-related tumors. Genetic mutations serve as hallmark fearures for diagnosing radiation damage. AT/RT development following sellar radiation has been documented once previously, but not in the case of prior pituitary adenoma. We present the first case, to our knowledge, of AT/RT following radiation for recurrent prolactinoma, and the first case in a patient with known MEN-1 syndrome.

Author Contributions

D.S. generated the idea for this case report and supervision. M.S.-R. and C.A. generated the original version of this report and all three authors edited multiple versions of the report. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

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Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

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