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Case Report

Primary Pineal Rhabdomyosarcoma: A Rare Case

Mihir Mohan Vaidya, Asha Sharad Shenoy[1], Naina Atul Goel[1]

Departments of Neuropathology and [1]Pathology, Seth G.S.M.C, Mumbai, Maharashtra, India

Abstract

Primary pineal rhabdomyosarcoma (RMS) is extremely rare, and only three cases have been reported so far. Here, we report a case of 12-year-old male who presented with complaints of diplopia and diminution of vision since 15 days. He also had left-sided facial paresis. Magnetic resonance imaging brain revealed a space-occupying lesion in the region of pineal gland. The patient underwent midline suboccipital craniectomy with excision of tumor. Microscopic examination revealed a highly cellular tumor with areas showing small round cells admixed with cells having abundant eosinophilic cytoplasm resembling rhabdomyoblasts and multinucleated giant cells. Differential diagnoses of pineal anlage tumor and primary RMS were considered. The tumor cells were positive for desmin while being negative for synaptophysin and glial fibrillary acidic protein. Myogenin was used to confirm the diagnosis of RMS, which showed focal nuclear positivity. INI1 was retained. All the markers for germ cell tumors were negative.

Keywords: *Desmin, myogenin, pineal gland, rhabdomyosarcoma*

Introduction

Rhabdomyosarcoma (RMS) is a malignant neoplasm with a predominantly skeletal muscle differentiation. Embryonal subtype is most commonly encountered in central nervous system (CNS) whereas alveolar subtype and a rhabdomyosarcomatous element in gliosarcoma are exceptionally rare.[1] Primary intracranial RMS is uncommon, and only 48 cases have been reported as per a recent case report.[2-4] Even more uncommon is the pineal region primary RMS. Only three cases have been reported in the literature so far excluding the two reports of rhabdomyosarcomatous transformation in a pineal region teratoma.[5,6] Here, we present a case of pineal region RMS in a young male patient.

Case Report

A 12-year-old male with no history of any chronic medical illness, presented with complaints of headache and diminution of vision in both eyes since 15 days. Headache was continuous and associated with vomiting. There was no history of convulsions, limb weakness, loss of consciousness, and bowel bladder disturbances. On examination, he was conscious and oriented to time, space, and person. His higher mental functions were normal. He had decreased visual acuity in both eyes, and there was left-sided facial paresis with a deviation of the tongue to the right side and loss of nasolabial fold on the left side. Rest of the cranial nerve examination were within normal limits, and there was no other sensory or motor deficit. Power was 5/5 in both upper and lower limbs, and the tone was normal. There were no cerebellar or meningeal signs.

Magnetic resonance imaging (MRI) brain revealed a heterogeneously enhancing space-occupying lesion in the pineal region, suggestive of a pineal gland tumor [Figure 1].

The patient underwent midline suboccipital craniectomy with excision of pineal region tumor.

Mass was received in neuropathology department in multiple small bits and fragments aggregating to 1.5 cm × 1 cm × 0.3 cm. Bits were grayish-white in color.

On microscopic examination, multiple biopsy bits showed a highly cellular tumor with areas showing small round cells with scanty cytoplasm and elongated ovoid nuclei. There was nuclear hyperchromasia. Also seen were areas with cells having abundant cytoplasm admixed with many giant cells having multiple nuclei with some

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Address for correspondence:
Dr. Asha Sharad Shenoy, 301, Arihant, 613-B, 15th Road, Khar, Mumbai - 400 052, Maharashtra, India.
E-mail: shenoyasha@yahoo.co.in

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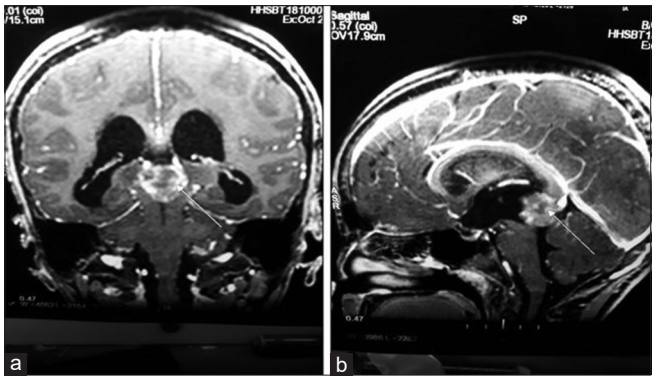

Figure 1: Magnetic resonance imaging brain T1 weighted postcontrast images in coronal (a) and sagittal (b) planes showing a heterogeneously enhancing mass in the region of pineal gland

showing prominent nucleoli. Brisk mitotic activity was noted. Large areas of necrosis and few areas of powdery calcification were also noted [Figure 2].

On morphology, due to a prominent small round cell component, a diagnosis of pineal parenchymal tumor was favored and in view of cells with more abundant cytoplasm and giant cells which suggested rhabdomyoblastic differentiation, a diagnosis of pineal anlage tumor was considered. RMS was also considered as the differential diagnosis. Immunohistochemistry was performed to confirm the nature of rhabdomyoblastic cells. Initially, immunohistochemistry for synaptophysin, glial fibrillary acidic protein (GFAP), and desmin was done.

On immunohistochemistry, tumor showed strong cytoplasmic positivity for desmin. All the cells, including small round cells, cells with more abundant cytoplasm and the giant cells, were positive for desmin. Synaptophysin and GFAP were negative in tumor cells which ruled out a pineal parenchymal tumor and a glial tumor, respectively. Considering the results of immunohistochemistry, a diagnosis of primary RMS of pineal region was favored; however, the diagnosis of a germ cell tumor, for example, teratoma with rhabdomyosarcomatous transformation was also considered. Further immunohistochemical workup was done. Myogenin was used to confirm the rhabdomyosarcomatous lineage of the tumor, which showed focal but definite nuclear positivity in the tumor cells [Figure 3]. Markers for germ cells tumors such as placental alkaline phosphatase (PLAP), alpha-fetoprotein (AFP), and cytokeratin (CK) were negative. Furthermore, on reviewing the MRI, no findings suggestive of a teratoma could be found. INI1 was retained which ruled out the possibility of atypical teratoid/rhabdoid tumor (AT/RT). Hence, considering the morphology and immunohistochemistry findings, a final diagnosis of Primary RMS of CNS was given.

Discussion

RMS originates from the skeletal muscle and is the most common childhood sarcoma.[7] 16%–40% of RMSs are

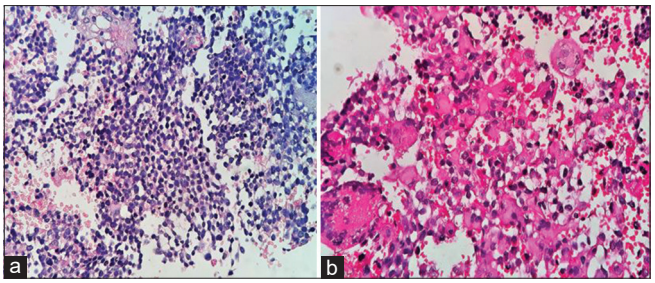

Figure 2: (a) Highly cellular tumor showing many small round cells with scanty cytoplasm and hyperchromatic nuclei (H and E, ×40). (b) Intermixed cells with abundant eosinophilic cytoplasm resembling rhabdomyoblasts and multinucleated giant cells (H and E, ×40)

known to arise in head and neck region nasal cavity and orbit are some of the common sites of head and neck RMS, while primary intracranial RMS is extremely rare.[2,7,8] Frontal lobe and cerebellum are the commonest reported sites of intracranial RMS.[3,4] Common pineal region tumors include pineal parenchymal tumors and the germ cell tumors,[1] RMS has been reported only three times at this site.[2,9,10]

The present case was a 12-year-old male patient. Pineal RMS reported by Ishi *et al*.[2] was also seen in a child (8-year-old female) whereas those reported by Scull *et al*.[9] and Lau *et al*.[10] were seen in adults (43-year-old female and 33-year-old female, respectively).

The chief complaints in the current case were headache and diminution of vision in both eyes since 15 days. Headache, nausea, ataxia, diplopia, and confusion were some of the symptoms observed in the other three reported cases of pineal RMS. None of the other cases reported any neurological deficit.[2,9,10] Our case had a left-sided facial paresis.

Microscopically, tumor had a prominent component of small primitive appearing cells with intermixed larger cells with moderate to abundant eosinophilic cytoplasm and multinucleated giant cells. No definite strap cells or cells with cross-striations were seen. According to the WHO 2016 classification of CNS tumors, strap cells and striations are only rarely seen in CNS RMSs and most tumors mainly show undifferentiated small cells.[1] Based on morphology, we considered (1) pineal anlage tumor which has an ectomesenchymal component in addition to a pineoblastoma and (2) RMS as the two differential diagnoses. Teratoma with rhabdomyosarcomatous differentiation[5,6] and ectomesenchymoma[11] are two other tumors in CNS that have a skeletal muscle differentiation. However, we could not find any other elements from the three-germ layers to consider the diagnosis of a teratoma. This finding was further corroborated by radiological review.

Our initial panel of antibodies consisted of synaptophysin, desmin, and GFAP. Majority of the tumor cells including the small cells and the giant cells showed uniform cytoplasmic desmin positivity.

All the tumor cells were synaptophysin and GFAP negative. Pineal parenchymal tumors[1] and the neural element of ectomesenchymoma[12,13] show positivity for synaptophysin, which were ruled out in this case. To confirm the diagnosis, a further panel was used consisting of myogenin to confirm the skeletal muscle origin and CK, PLAP, and AFP to rule out a germ cell component. Myogenin, which is a specific marker for RMS,[14] showed focal nuclear positivity. Alveolar RMS shows extensive nuclear staining for myogenin with positivity in more than 75% of tumor cells in most cases, whereas it is less uniform and focal in embryonal RMS.[14,15] All the markers for germ cell tumor were negative. AT/RT is heterogeneous lesions which in majority of cases contain a population of classic rhabdoid cells with abundant eosinophilic cytoplasm, eccentric vesicular nuclei with prominent eosinophilic nucleoli and globular eosinophilic cytoplasmic inclusion. INI1 immunostaining is a sensitive and specific test for diagnosis of AT/RTs, in which there is a loss of nuclear expression of SMARCB1.[1] We did not find intracytoplasmic inclusions in any of our cells with rhabdoid morphology, and INI1 was expressed in the tumor cells hence ruling out AT/RT. Thus, the final diagnosis of primary RMS of pineal region was considered.

Ishi *et al*.[2] in their reported case, found differentiated spindle cells with eosinophilic cytoplasm resembling striated muscle cells. Lau *et al*.[10] also found elongated strap cells and globoid cells with eccentric nuclei resembling rhabdomyoblasts. They also reported multinucleated myotube-like structures which were focally seen in our case. Scull *et al*.[9] described a pleomorphic tumor with malignant spindle cells and large polygonal tumor cells with rhabdomyoblastic morphology.

All the three case reports described positive cytoplasmic staining for Desmin,[2,9,10] with Ishi *et al*.[2] also reporting a part positivity in immature cells. In addition to Desmin, Scull *et al*.[9] reported positivity for myogenin, INI1, and muscle-specific actin, whereas Lau *et al*.[10] reported positivity for myogenin and myoD1. Synaptophysin, NSE, GFAP, CD117, PLAP, CK, and OCT3/4 were some of the negative markers reported by these three case reports[2,9,10] [Table 1].

Findings of the present case are compared with the other reports, as shown in Table 1.

Scull *et al*.[9] and Lau *et al*.[10] reported poor outcome for their patients with survival of only 4 months and 5 months after the diagnosis, respectively. Ishi *et al*. used an aggressive multimodal form of the treatment including surgery, chemotherapy, radiation, and high-dose chemotherapy (HDC) followed by autologous peripheral blood stem cell transplantation (HDC). Their patient was alive 30 months after diagnosis with no evidence of tumor.[2] In the present case, the patient was unfortunately lost to follow-up following the surgery [Table 2].

Conclusion

While primary RMS of the pineal gland is extremely rare, skeletal muscle differentiation can be seen in other tumors encountered at this site, for example, pineal anlage tumors

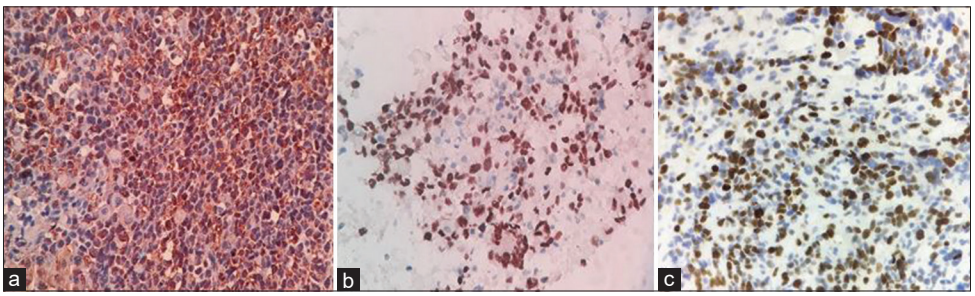

Figure 3: (a) Positive cytoplasmic staining for desmin is seen in the tumor cells (Desmin, ×40). (b) Tumor cells show positive nuclear staining for myogenin (Myogenin, ×40). (c) INI1 expression was retained in the tumor cell nuclei. Tumor was negative for synaptophysin, glial fibrillary acidic protein, pan cytokeratin, alpha-fetoprotein, and placental alkaline phosphatase (INI1, ×40)

Table 1: Comparison of the clinicopathological features of the current case with other reported cases

Case	Age (years)	Sex	Clinical features	Microscopy	Positive stains	Negative stains
Ishi *et al*.[2]	8	Female	Headache, nausea	Spindle cells resembling striated muscle cells	Desmin	PLAP, OCT3/4, synaptophysin, chromogranin, neurofilament
Scull *et al*.[9]	43	Female	Headache, ataxia, diplopia	Spindle cells and polygonal cells with rhabdomyoblastic morphology	Desmin, myogenin, muscle-specific actin, INI1	Pan CK, CAM5.2, PLAP, Synaptophysin, Chromogranin
Lau *et al*.[10]	33	Female	Headache, nausea, confusion	Strap cells, rhabdomyoblasts, multinucleate cells	Desmin, myogenin, Myo D1, INI1	NSE, CD117, Synaptophysin (in tumor cells), GFAP, PLAP
Present case	12	Male	Headache, diminution of vision	Small round cells, larger cells, and multinucleate cells	Desmin, myogenin, INI1	Synaptophysin, GFAP, Pan CK, PLAP, AFP

GFAP – Glial fibrillary acidic protein; CK – Cytokeratin; PLAP – Placental alkaline phosphatase; AFP – Alpha-fetoprotein

Table 2: Comparison of the treatment modalities and the outcome with other reported cases

Case	Treatment	Outcome
Ishi *et al*.[2]	Surgery, chemotherapy, radiation, high-dose chemotherapy, stem cell transplantation	No recurrence at 30 months
Scull *et al*.[9]	Surgery	Rapid local recurrence
Lau *et al*.[10]	Surgery and chemotherapy	Rapid intracranial failure
Present case	Surgery	Lost to follow-up

and rhabdomyosarcomatous differentiation in teratomas. Immunohistochemistry is valuable in differentiating these entities. In the present case, desmin and myogenin positivity in the tumor cells retained INI1 along with negative synaptophysin, GFAP, Pan-CK, PLAP, and AFP was considered to be diagnostic of RMS.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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