Rare disease

Ependymoblastoma in an adult: a diagnostic challenge on cytology

Sonal Amit, Priyanka Chand, Chayanika Pantola, Asha Agarwal

Department of Pathology, GSVM Medical College, Kanpur, India

Correspondence to Dr Sonal Amit, drsonalamit@gmail.com

Summary

Ependymoblastoma is a rare, highly malignant brain tumour considered by most to be a subtype of primitive neuroectodermal tumour manifesting in young children. The authors present an unusual case of ependymoblastoma occurring in an 18-year-old female, one of the oldest patients reported with this tumour. The crush smears were highly cellular comprising singly scattered small, round immature cells with fine granular chromatin. The paraffin sections showed a tumour composed of uniform, small-sized, primitive cells forming well defined multi-layered rosettes with prominent mitoses. The tumour cells exhibited diffuse Vimentin and focal glial fibrillary acidic protein reactivity. A few cells showed S-100 reactivity. The patient underwent radiotherapy following complete tumour debulking but, succumbed to the disease within 2 months of diagnosis.

BACKGROUND

Ependymoblastoma is considered to be a malignant glioma with ependymal differentiation. This rare tumour occurs in very early life and shows rapid growth and diffuse infiltration through the leptomeningeal space.¹ The tumour is presumed to arise from periventricular neuro-epithelial precursor cells.² The revised version of WHO of central nervous system (CNS) tumours places ependymoblastoma in a group of primitive neuroectodermal tumours (PNET) with the capacity to differentiate into ependymal cells. Within this classification, ependymoblastoma has clear histological characteristics which allow its differentiation from medulloblastoma and other PNETs.³ Although there have been sporadic case reports of this rare tumour occurring in older age, description of cytological features has been extremely scarce. We conclude that rare cases of ependymoblastoma may be encountered in adults. Further, the cytological features are sufficient to suggest a diagnosis of embryonal tumour yet, not specific for a diagnosis of ependymoblastoma.

CASE PRESENTATION

An 18-year-old girl sought medical help for gradually worsening left-sided headache and diplopia over period of 3 months associated with two episodes of generalised convulsions. There was no history of vomiting, other focal neurological deficit or trauma. On neurological examination, patient was alert, well oriented with no sensori-motor deficit. Ophthalmic examination revealed medial deviation of left eye along with papilloedema in the left eye fields.

Contrast enhancing CT scan disclosed a large, circumscribed, heterogeneous space occupying lesion in the left temporo-frontal region with minimal peri-lesional oedema. Focal cystic component and calcified dots were noted and the lesion showed heterogeneous contrast enhancement. There was midline shift to right side with partial obliteration of the basal cisterns (figure 1).

Subsequent MRI localised the 5×7×4.5 cm lesion to left frontal lobe, with extension into the adjacent temporal and parietal lobes. The lesion was predominantly hyperintense on T2 WIs, T2 FLAIR and hypointense on T1 WIs. Based on CT and MRI findings, a diagnosis of left-sided anaplastic fronto-temporal glioma was suggested. The patient underwent open craniotomy and total tumour debulking was done.

The specimen was received in two containers; a small part of tissue in normal saline for crush preparation and the rest in 10% buffered formalin for histopathological

Figure 1 CT scan showing large heterogeneous space occupying lesion in temporo-frontal area with cystic component and few calcified dots. Medial deviation to right is also seen.

Figure 2 Crush cytology smears showing highly cellular tumour composed of monotonous population of singly lying primitive cells with high nucleocytoplasmic ratio and fine granular chromatin. A mitotic figure is also seen (arrow) (HE $\times 400$).

Figure 3 Histopathological section showing tumour composed of ependymoblastic rosettes and canals (HE $\times 100$).

examination consisting of few irregular grey white soft tissue pieces altogether measuring 2 $\times$ 1 cm.

The H&E stained crush smears were highly cellular comprising dispersed population of uniform round to oval cells. The cells were primitive looking with high

nucleocytoplasmic ratio, ill-defined cytoplasm and round nuclei with fine granular chromatin. Nuclear overlapping, moulding and atypical mitotic figures were seen (figure 2). A cytological diagnosis of PNET was suggested. The histopathological sections revealed tumour of high cellularity

Figure 4 High power view showing endymoblastic rosettes composed of concentric arrangement of immature small round tumour cells around empty lumina with conspicuous juxtaluminal mitoses (arrow) (HE $\times 400$).

composed of small sized cells arranged in diffuse sheets punctuated by true rosettes and canals characterised by radial arrangement of cells around empty lumen with conspicuous juxtaluminal mitoses. The tumour cells were poorly differentiated with granular chromatin (figures 3 and 4). Immunohistochemistry revealed diffuse positivity for Vimentin and focal glial fibrillary acidic protein (GFAP) reactivity. Perinuclear S-100 protein reactivity was seen in few cells. Final diagnosis of endymoblastoma was thus rendered and patient underwent postoperative radiotherapy.

OUTCOME AND FOLLOW-UP

The patient underwent postoperative radiotherapy following tumour debulking but, succumbed to the disease within 2 months of diagnosis.

DISCUSSION

The term 'endymoblastoma' was used originally by Bailey and Cushing,⁴ who proposed that the tumours arising from endyma should be divided into two subgroups namely, endymoma and endymoblastoma. However, subsequently this subclassification was discarded by its original proponents as both these entities were devoid of mitotic activity and shared blepharoplasts characteristic of adult endymal elements.^{1 5} Meanwhile, the term 'endymoblastoma' was retained⁵ and redefined by Rubinstein as a special type of embryonal CNS neoplasm occurring in young individuals wherein the cytological features of a primitive highly cellular neuroectodermal tumour are associated with the presence of numerous true or endymal rosettes.^{1 6} The recent revision of the WHO Classification of CNS tumours places endymoblastoma in a group of primitive neuroectodermal tumours with the capacity to differentiate along one or more cell lines, in this case with endymal differentiation.³

Clinically, these tumours display extremely aggressive course with tendency toward local invasion, recurrence and infiltration of leptomeninges and correspond to WHO grade IV³ with a median survival of 1 year.² Endymoblastoma arise in early life as do other PNETs, with a mean age at presentation of 4.7 years.¹ However, there have been reports of these tumours occurring in older age group. Dorhman *et al*⁷ and Shu-Hang *et al*² have reported endymoblastoma occurring in patients aged 18 years and 14 years respectively while, Mork and Rubinstein⁵ reported two other cases occurring in 16 and 36 year old individuals. A case of disseminated primary leptomeningeal endymoblastoma was reported by Wada *et al*¹ in a 17-year-old girl. Thus, the present case falls in the same category of rare cases of endymoblastoma presenting in older age group.

These neoplasms are usually large and well circumscribed with younger individuals tending to attain a larger tumour size. Focal necrosis, haemorrhage and cystic change may be seen.⁵ Radiologically, the presence of a large clearly demarcated supratentorial mass with remarkably minimal oedema and heterogeneous contrast enhancement suggests the possibility of this lesion.^{2 8} Endymoblastomas generally relate to the ventricles, although they do occur at other sites.³ Mork and Rubinstein,⁵ in a review of 12 endymoblastoma cases found only four tumours related to the ventricular lining while, seven others were clearly separated from the ventricular wall. These lesions have presumably arisen from ectopic endymal cell nests that are frequently found in the periventricular white matter.⁵ In the present case, the temporo-frontal location of the tumour without any relation to the ventricles represents a similar histogenesis.

The histological diagnostic feature of endymoblastoma is its dense cellularity with numerous distinctive multi-layered rosettes formed by concentric arrangement

of cellular rings around small round lumina.^{3 5 9} The tumour cells are poorly differentiated, oval to spindle shaped with ill-defined cytoplasm and wispy polar processes.⁵ Features which identify these tumours as embryonal are the small cell size, uniform appearance and round or ovoid nuclei showing frequent mitoses.⁹ The structure of ependymoblastic rosette corresponds to the later phase of neural tube development characterised by multilayering of cells and abundant mitotic activity in juxtaluminal position.^{5 9}

Though an established entity, there is extreme paucity of literature regarding the cytopathological aspects of ependymoblastoma. The aspirates in ependymoblastoma are highly cellular and though rosettes may be seen, they are generally rare.¹⁰ The cytological features in the present cases tallied with those of Kaoru *et al*¹¹ who reported a case of ependymoblastoma of the nasal cavity wherein the imprint smears revealed small round uniform cells with scant cytoplasm and fine granular nuclei. However, unlike their case, in the present case rosettes were not appreciated on cytology although they were conspicuous in histological sections.

Immunohistochemical profile revealed S-100 and Vimentin positivity in all cases reviewed by Cruz-Sanchez *et al*.^{9 12} The authors observed that, in contrast to medulloblastomas, vimentin reactivity in ependymoblastomas was present in most cells throughout the tumour and its intensity was stronger, indicating a later stage of maturation in the latter group. GFAP was found to be absent or only sparsely positive in few tumour cells.¹² However, glial or neural differentiation using immunohistochemical markers was not detected in the case of primary leptomeningeal ependymoblastoma reported by Wada *et al*.¹ In the present case, diffuse and intense tumour cell positivity for vimentin was seen with few cells showing GFAP reactivity and only sparse number of cells demonstrated neural differentiation in the form of perinuclear S-100 positivity.

Ependymoblastomas must be distinguished from anaplastic ependymomas. Ependymoblastomas do not have well developed pseudorosettes and seldom have the degree of cytoplasmic or nuclear pleomorphism characteristic of the anaplastic ependymomas. Necrosis may be present in both tumour types although, geographic and pseudopalisading patterns of necrosis are only found in anaplastic ependymomas.¹³ Medulloepitheliomas may contain ependymoblastoma type rosettes but they can be distinguished by their diagnostic neuroepithelium characterised by an outer basement membrane arranged in tubular, canalicular and papillary patterns. Medulloblastoma are differentiated by their cerebellar location and characteristic Homer-Wright rosettes which lack a central lumen.³

Recently, Judkins and Ellison¹⁴ have challenged the existence of this entity. They reviewed 14 embryonal brain tumours and found ependymoblastic rosettes as a

key diagnostic feature in 79% tumours while remaining showed similar rosettes in a setting of other typical embryonal tumours. The authors believe that ependymoblastoma as a diagnosis is neither precise nor specific and it is time for this diagnosis to depart from the lexicon of neuropathology. Although retained in latest WHO Classification, such experience may pave way for future modifications in diagnostic categorisation of these tumours.

Learning points

- ▶ Though predominantly a tumour of young children, rare ependymoblastoma cases may occur in adults.
- ▶ The cytology of ependymoblastoma is diagnostically challenging since it recapitulates other embryonal tumours.
- ▶ Definite distinction from other embryonal tumours is achieved only on histopathology by the presence of characteristic multi-layered rosettes.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. Wada C, Kurata A, Hirose R, *et al*. Primary leptomeningeal ependymoblastoma. Case report. *J Neurosurg* 1986;**64**:968–73.
2. Shu-Hang Ng. Ependymoblastoma: CT and MRI demonstration. *Clin J Radiol* 2002;**27**:21–5.
3. Louis DN, Ohgaki H, Weistler OD, *et al*. *WHO Classification of Tumors of the Central Nervous System*. Fourth edition. Lyon: IARC Press 2007:145–6.
4. Bailey P, Cushing H. *A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis*. Philadelphia, PA: J B Lippincott Co 1926.
5. Mørk SJ, Rubinstein LJ. Ependymoblastoma. A reappraisal of a rare embryonal tumor. *Cancer* 1985;**55**:1536–42.
6. Rubinstein LJ. The definition of the ependymoblastoma. *Arch Pathol* 1970;**90**:35–45.
7. Dohrmann GJ, Farwell JR, Flannery JT. Ependymomas and ependymoblastomas in children. *J Neurosurg* 1976;**45**:273–83.
8. Dorsay TA, Rovira MJ, Ho VB, *et al*. Ependymoblastoma: MR presentation. A case report and review of the literature. *Pediatr Radiol* 1995;**25**:433–5.
9. Cruz-Sanchez FF, Hausteir J, Rossi ML, *et al*. Ependymoblastoma: a histological, immunohistological and ultrastructural study of five cases. *Histopathology* 1988;**12**:17–27.
10. Galloway M, Thom M. Brain and cerebrospinal fluid. In: Gray W, Kocjan G, eds. *Diagnostic Cytopathology*. Second edition. Philadelphia, PA: Churchill Livingstone 2003:965.
11. Kaoru S, Akiko H, Kumiko O, *et al*. A case report of ependymoblastoma of the nasal cavity. Cytological, histopathological and ultrastructural study and review of the literatures. *J Jpn Soc Clin Cytol* 1999;**38**:151–6.
12. Cruz-Sánchez FF, Rossi ML, Hughes JT, *et al*. Differentiation in embryonal neuroepithelial tumors of the central nervous system. *Cancer* 1991;**67**:965–76.
13. Lopes MBS, Vandenberg SR. Tumours of the central nervous system. In Fletcher CDM, ed. *Diagnostic Histopathology of Tumours*. Third edition. Philadelphia, PA: Churchill Livingstone 2007:1702.
14. Judkins AR, Ellison DW. Ependymoblastoma: dear, damned, distracting diagnosis, farewell!*. *Brain Pathol* 2010;**20**:133–9.

This pdf has been created automatically from the final edited text and images.

Copyright 2011 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Amit S, Chand P, Pantola C, Agarwal A. Ependymoblastoma in an adult: a diagnostic challenge on cytology. *BMJ Case Reports* 2011; 10.1136/bcr.09.2011.4746, date of publication

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow