Human Pathology (2012) **43**, 299–302

ELSEVIER

Human PATHOLOGY

www.elsevier.com/locate/humpath

Case study

Ectomesenchymoma with t(1;12)(p32;p13) evolving from embryonal rhabdomyosarcoma shows no rearrangement of *ETV6*☆

Sinead Howley MSc[a], Deirdre Stack PhD[a], Thomas Morris BSc[b], Michael McDermott MBBCh[c], Michael Capra MBBCh[d], David Betts BSc[b], Maureen J. O'Sullivan MBBCh, MD[a,c,*]

[a]*National Children's Research Centre, Our Lady's Children's Hospital, Crumlin, Dublin 12, Ireland*
[b]*National Centre for Medical Genetics, Our Lady's Children's Hospital, Crumlin, Dublin 12, Ireland*
[c]*Department of Pathology, Our Lady's Children's Hospital, Crumlin, Dublin 12, Ireland*
[d]*Department of Oncology, Our Lady's Children's Hospital, Crumlin, Dublin 12, Ireland*

Received 7 January 2011; revised 15 February 2011; accepted 11 March 2011

Keywords:
Ectomesenchymoma;
Pediatric;
Rhabdomyosarcoma;
Mesenchyme;
Ganglion cell;
Karyotype

Summary Ectomesenchymoma is a rare mesenchymal malignancy occurring mainly in the pediatric population. The hallmark diagnostic features are a combination of sarcoma, usually rhabdomyosarcoma (RMS) with admixed ganglion cells. The lesion arises either in soft tissues or the cranial cavity, and outcomes vary considerably. Current knowledge about the genetics and biology of ectomesenchymoma is extremely limited with only 4 published karyotypes, showing overlaps only in trisomies 2, 8, and 11. Here, we describe a case with genetic findings that, in conjunction with preexisting observations, offer some additional insights into the genetic aberrations of ectomesenchymoma.

1. Introduction

We report a case of ectomesenchymoma arising in a girl initially diagnosed with botryoid embryonal rhabdomyosarcoma (RMS) of the vagina and treated for this with a contemporary rhabdomyosarcoma protocol. The ectomesenchymoma showed karyotypic changes including t(1;12)(p32;p13). Existing genetic data on ectomesenchymoma are sparse and include only 1 prior case report including karyotype with t(12;15)(p13;q24), not further characterized [1].

2. Materials and methods—case report

Our patient presented at age 6 months with a mass protruding from her vagina. Biopsy was taken and showed classic histology of botryoid embryonal rhabdomyosarcoma (see histology below). Imaging revealed a vaginal mass and separate paraaortic lesion together with enlarged bilateral iliac nodes. After 6 months of RMS-directed chemotherapy (ifosfamide, vincristine, actinomycin, doxorubicin), as per the EpSSG RMS 2005 protocol, she had a macroscopic complete resection of the pelvic/vaginal mass, including a paraaortic abdominal lesion. Histology showed viable

☆ Funding Support: Children's Medical and Research Foundation, Dublin, Ireland and a grant from the National Children's Research Centre, Dublin, Ireland to M.J.O. [grant E/08/1].

* Corresponding author. Histology Laboratory, Our Lady's Children's Hospital, Crumlin, Dublin 12, Ireland.
E-mail address: maureen.osullivan@tcd.ie (M. J. O'Sullivan).

0046-8177/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1016/j.humpath.2011.03.010

rhabdomyosarcoma tumor cells in at least 50% of the resected tumor. Chemotherapy was intensified (irinotecan, topotecan, vincristine, and carboplatin in combination) as a result of this poor response, but she developed progressive recurrent abdominopelvic tumor requiring further biopsy 4 months later. Histology at this time showed a spindle cell tumor containing scattered ganglion cells. Evolution into ectomesenchymoma was diagnosed, and therapy was altered to include cisplatin and etoposide. Progression of the abdominopelvic tumor was confirmed by fine needle aspiration biopsy at 12 months post-initial diagnosis and subsequent management was with palliative intent until the patient's demise 3 months later.

3. Results—pathology and genetics

Initial biopsy was that of classic embryonal rhabdomyosarcoma with no trace of ganglionic differentiation. The growth pattern was botryoid with a well-developed cambium layer present (Fig. 1A). The posttreatment resection specimen was multilobular with a whorled, tan cut surface appearance with focal fleshy brown areas. Microscopy showed some evidence of cytodifferentiation compared with the pretreatment biopsy and only minimal necrosis. The tumor contained scattered ganglion-like cells. Nodules of primitive, undifferentiated cells were present at the peripheries of the mass. These primitive cells showed strong reactivity for myogenin and MyoD1 along with desmin. Ki-67 stained a large fraction of nuclei. Biopsy from the bladder relapse showed neuroblastic tumor containing ganglion cells, neuropil, and a prominent Schwannian component also, effectively ganglioneuromatous tissue (Fig. 1B). The cells showed strong reactivity for CD56; however, a proportion of cells also stained for desmin. Subsequent biopsy of residual tumor at the base of bladder showed large cells with considerable anaplasia in addition to small primitive cells. The small primitive cells stained with myogenin and CD56, whereas the larger anaplastic cells were positive for CD56 and NB-84 but lacked any reactivity for muscle markers. The features effectively confirmed a biphenotypic ectomesenchymoma. Cytogenetic evaluation of the bladder nodule showed der(1)t(1;12)(p32;p13) del(5)(q13q22), der(12)t(p32;q13)[9]/46,XX[3] (Fig. 2). Fine needle aspiration biopsy of a new umbilical nodule at 12 months post-initial diagnosis showed recurrent primitive malignant tumor.

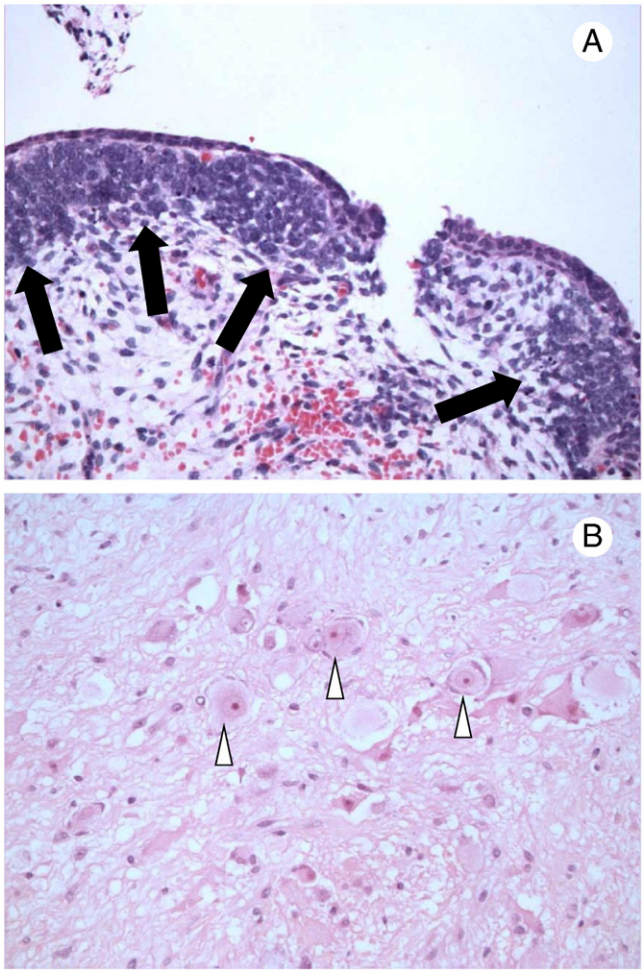

Fig. 1 A, Biopsy of the vaginal mass shows a botryoid growth pattern, with a well-developed cambium layer (black arrows) present. B, Histology of the relapsed neuroblastic tumor containing ganglion cells (white arrowheads), in a Schwannian stroma, amounting to ganglioneuromatous tissue.

4. Discussion

Ectomesenchymoma is a rare malignancy of soft tissues comprising a combination of malignant mesenchyme, most commonly rhabdomyosarcoma, with admixed neural elements and, occasionally, with additional heterologous mesenchymal elements present also, and occurring predominantly in the pediatric population [2,3]. Ectomesenchymoma is thought to arise from neural crest cells, which might serve to explain the divergent differentiation. Per the World Health Organization classification, ectomesenchymoma belongs to the rhabdomyosarcoma group; and this categorization is corroborated by a genetic profiling study suggesting that ectomesenchymoma shows rhabdomyosarcomatous differentiation [4], although an isolated intracranial case was reported to segregate with malignant peripheral nerve sheath tumor (MPNST) rather than a variety of other pediatric solid malignancies including RMS [5]. Ectomesenchymoma may occur as an intracranial primary or in the soft tissues including peripheral and deep seated alike. A review of 39 cases showed a preponderance in the first decade of life (81%), with a 17:13 female-to-male ratio. Eighty two percent had rhabdomyosarcomatous elements, whereas 29% contained ganglion cells [6].

Although ectomesenchymoma may represent a primary diagnosis, cases also exist where initial diagnosis was of rhabdomyosarcoma with either metastasis posttherapy [7] or relapse posttherapy [8], then declaring itself as ectomesenchymoma. In the former setting, electron microscopic