

Case Report

Recurrent primary endobronchial fetal rhabdomyoma: a case report and literature review

Stefano Marletta¹, Anna Caliò¹, Adele Fioravanzo¹, Enrico Cavallo¹, Evelin Torresani¹, Federica Zampieri¹, Eliana Gilioli²

¹ Department of Diagnostics and Public Health, Section of Pathology, University of Verona, Verona, Italy;

² Department of Pathology and Diagnostics, University and Hospital Trust of Verona, Verona, Italy

Summary

Fetal rhabdomyoma is an extremely rare benign rhabdomyoblastic tumor with myotube-like differentiation, mainly arising on mucosal surfaces of the head and neck region of both children and young patients, almost invariably definitively treated with surgical excision. Herein the case of a male adult suffering from a recurrent fetal rhabdomyoma primary involving the bronchial structures is reported, along with a detailed literature review. This is the first fetal rhabdomyoma described to originate in such a localization; furthermore, an 11-year interval period between the first lesion and the recurrent one has never been reported.

Key words: skeletal muscle differentiation, benign mesenchymal neoplasm, fetal rhabdomyoma, endobronchial, recurrence

Introduction

Rhabdomyomas are benign mesenchymal neoplasms showing skeletal muscle differentiation. Regarding their localization, rhabdomyomas are generally classified into two main groups: cardiac rhabdomyomas and extracardiac rhabdomyomas. These latter are fairly more uncommon and further divided into three clinically and morphologically different subtypes: adult type, which commonly affects the head and neck region of elder people; fetal type, a lesion usually growing in the head and neck region mainly in children; genital type, a polypoid benign tumor that has almost uniquely been described in the external genitalia and the vagina of middle-aged women ¹. Firstly described by Dehner, Enzinger and Font in 1972 ², fetal rhabdomyoma is a benign rhabdomyoblastic tumor showing myotube-like differentiation, therefore resembling primitive skeletal muscle fibers during fetal development. According to their histologic features, fetal rhabdomyomas are further classified as myxoid or classic fetal rhabdomyomas and as intermediate, cellular, or juvenile fetal rhabdomyomas, being often found in the head and neck region of children and youngsters. Despite their rarity, fetal rhabdomyomas should always be of concern for pathologists, as they may often resemble embryonal rhabdomyosarcoma. Since their benign biological behavior, surgical excision is generally curative ¹.

Here we describe the case of a male adult diagnosed with a primary endobronchial fetal rhabdomyoma that recurred 11 years after the excision. This is the first fetal rhabdomyoma arising from such a localization, and also the one with the widest recurrence interval ever reported.

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Correspondence

Stefano Marletta
Department of Diagnostics and Public Health,
Section of Pathology, University of Verona,
p.le L.A. Scuro 10, 37134 Verona, Italy
Tel.: +39 045 8127458
Fax: +39 045 8027136
E-mail: stefano.marletta92@gmail.com

Conflict of interest

The Authors declare no conflict of interest.

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Case report

A 59-years-old man accessed Verona University's hospital in May 2007 for cough and breath difficulties. A tracheobronchial endoscopic examination revealed a polypoid mass occluding the main left bronchus that was endoscopically resected. Not suffering any other main respiratory issues, the patient was then dismissed. Grossly, the lesion appeared as a gray-whitish 1.7 cm soft polyp mass with a glistening cut surface. Samples obtained were fixed in 10% formalin and embedded in paraffin. Paraffin-embedded tissue blocks were cut into 2- to 3- μ m sections and stained using hematoxylin-eosin.

Morphologically, beneath a well-defined layer of ciliated cylindrical epithelial cells, the lesion was made up of spindle and starry-shaped benign-looking cells, diffusely dispersed within an edematous and vascular stroma, this latter one largely overcoming the cellular population (Fig. 1). Neoplastic cells were reminiscent

of fetal myotubes, as they showed bipolar or sometimes unipolar finely tapered eosinophilic cytoplasmic processes, recalling cross striations of skeletal muscle fibers, and small uniform nuclei with delicate chromatin and inconspicuous nucleoli. No mitoses nor necrosis were spotted. Immunohistochemical stainings were performed with the following antibodies: smooth muscle actin (clone 1A4, dilution 1:250; Dako), muscle-specific actin (clone HHF35, dilution 1:1000, Dako), CD34 (clone QBEND/10, dilution 1:200; Novocastra), desmin (clone D33, dilution 1:1000; Dako), GFAP (clone 6F2, dilution 1:500; Dako), Bcl-2 (clone EP36, dilution 1:100; Epitomics), and S100 (polyclonal rabbit, dilution 1:3000; Dako). The neoplastic cells revealed a myogenic differentiation, as they expressed muscle-specific actin, smooth muscle actin and desmin but neither GFAP nor S100, ruling out a neural-derived lesion. Although morphological and immunohistochemical data suggested a benign neoplasm with myogenic differentiation, a definitive histological diagnosis was



Figure 1. Low (A) and high (B) power magnification showing fascicles of tumor cells, highlighted by the arrows, embedded in a myxoid stroma.

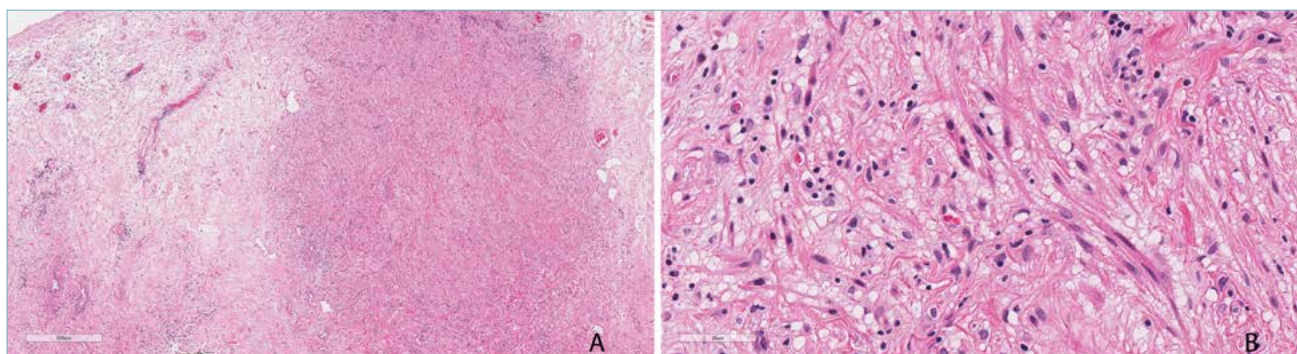


Figure 2. Low (A) and high (B) power view of the recurrent lesion with a cell-poor area, characterized by a few oval rhabdomyoblastic cells embedded within a loose connective tissue, intermingled with a more cellular focus of spindle cells haphazardly arranged in irregular bundles.

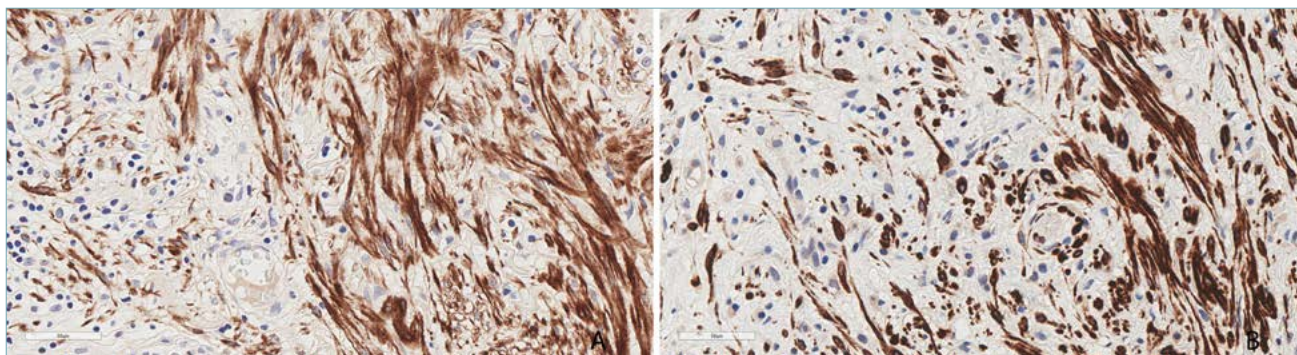


Figure 3. Myogenic differentiation of the recurrent lesion is confirmed by positive staining for muscle specific actin (A) and desmin (B).

not given due to the challenging and rare pathological findings and the lesion was defined as a mesenchymal neoplasm with a likely indolent biological behavior.

In March 2018, 11 years after his first diagnosis, the patient experienced another episode of ongoing breathing difficulties for which a further endoscopic examination was required: the main left bronchus was filled with a multilobed-looking, smooth, highly vascular lesion which jutted into the lower lobar bronchus, occluding it and causing the distal airways to collapse. No other airway abnormalities were observed. Evaluation of bronchial lavage fluid cytology revealed abundant of macrophages and cylindrical hairy cells without atypia. Biopsies of the lesion were not diagnostic as they only showed normal bronchial mucosa with chronic inflammation and squamous metaplasia. Therefore, another endoscopic exam was performed to remove the lesion, which was then sent to the Pathology Department for the histological diagnosis.

This new polypoid lesion was grossly similar to the previous one, being of 1.5 cm in its greatest dimension, and shared utterly overlapping morphological (Fig. 2A, B) and immunohistochemical (Fig. 3A, B) features with it: therefore, along with the findings of the primary lesion, a diagnosis of recurrent endobronchial fetal rhabdomyoma was finally established.

Discussion

Rhabdomyomas are benign neoplasms showing skeletal muscle differentiation. Unlike most other soft tissue tumors, rhabdomyomas are strikingly outnumbered by their malignant counterpart, rhabdomyosarcomas, only accounting for more or less 2% of all tumors with striated muscle differentiation. Although

they are rare, these tumors are generally classified as cardiac or extracardiac rhabdomyomas¹. As previously mentioned, fetal rhabdomyomas commonly involve the head and neck region, but they have been rarely reported in other localizations, summarized in Table I: despite such descriptions being almost anecdotal, fetal rhabdomyomas have been detected in many different anatomic sites, arising from both parietal regions, ranging from the upper arms^{3,4} to the retroperitoneal space^{5,6}, and from deep visceral organs, for instance the heart⁷⁻⁹ and the urinary bladder¹⁰⁻¹². Interestingly, apart from the actual study, only 5 other cases have been described to affect adults so far^{4,12-15}. As far as cardiac and vulvar involvement is concerned, it is mandatory to say that the mentioned lesions were true fetal-type rhabdomyomas, as they strikingly matched the diagnostic criteria of World Health Organization (WHO), and not cardiac-type and genital-type rhabdomyomas, respectively, which fairly more commonly involve the same regions. The endobronchial origin of fetal rhabdomyomas has not been reported and this is the first published case about this localization.

Fetal rhabdomyomas are slowly growing processes, with little or any change in size or histologic features, beside interstitial fibrosis, even in long-standing lesions. Therefore, complete excision is usually curative¹. Incomplete resection is probably to blame for the extremely rare but well-documented examples of recurrent fetal rhabdomyomas; including the actual study, there are only 7 reports of recurrent fetal rhabdomyomas in the English literature, listed in Table II. As in our case, recurrent tumors are usually of similar size or smaller than the previous ones, suggesting that incomplete resection is probably to blame for these extremely rare but well documented examples of recurrent fetal rhabdomyomas¹⁶⁻¹⁸. Namely, while original tumors may be quite variable in their size,

Table I. Summary of reported cases of fetal rhabdomyoma arising outside the head and neck region.

Case report	Publication year	Patient demographics (M/F, age)	Localization
Dehner et al.	1972	M, 1 y.o. M, 1 y.o.	Costal margin Chest wall and axilla
Dahl et al.	1976	F, /	Thigh Chest wall
Szadowska et al.	1979	/	Urinary bladder
Di Sant'Agnese et al.	1980	M, 54 y.o. M, 3 y.o.	Thigh Stomach
Konrad et al.	1982	F, Newborn	Abdominal wall
Whitten et al.	1987	F, Newborn	Retroperitoneum
Dodat et al.	1987	M, Child	Urethra
Di Santo et al.	1992	F, 6 y.o.	Mediastinum and retroperitoneum
Hardisson et al.	1996	M, 15 y.o.	Retroperitoneum
Lapner et al.	1997	F, Newborn	Perianal
Osgood et al.	1998	/	Upper arm
Sencan et al.	2000	M, 8 y.o.	Paratesticular
Kurzrock et al.	2003	M, 1 y.o.	Paratesticular
Gao et al.	2004	F, 3 month-old	Heart
Abdullaev et al.	2009	M, Child	Urethra and Urinary Bladder
Premalata et al.	2009	M, 9 y.o.	Thigh
Viscardi et al.	2009	2 M, Newborns	Heart
Yang et al.	2011	M, 17 y.o.	Mediastinum
Pastorino et al.	2012	F, 40 y.o.	Chest wall
Harder et al.	2013	M, 68 y.o.	Cerebellar pontine angle
Zheng et al.	2013	M, 12 y.o.	Paratesticular
Diociaiuti et al.	2015	F, 1 y.o.	Chest wall
Martos-Moreno et al.	2016	F, Newborn	Vulva
Kayali et al.	2017	F, Newborn	Heart
González-Pérez et al.	2018	M, 87 y.o.	Urinary bladder
Hauer et al.	2019	M, 31 y.o.	Upper arm
Actual study	2020	M, 59 y.o.	Bronchus

Table II. Summary of reported cases of recurrent fetal rhabdomyomas.

Case report	Publication year	Patient demographics (M/F, age)	Site	Recurrency temporal setting
Konrad et al.	1983	M, 9 y.o.	Eyebrow	7 months
Kodet et al.	1991	F, 1 y.o.	Tongue	10 and 22 months, with rhabdomyosarcomatous features
Kapadia et al.	1993	M, 5 month-old	Cheek	3 months
Smith et al.	1996	M, Newborn F, 3 y.o.	Neck Preauricular	10 years 4 months
Wang et al.	1996	M, 3 y.o.	Neck	5 years
Valdez et al.	2006	/, Newborn	Head and Neck	14 and 18 months
Actual study	2020	M, 59 y.o.	Bronchus	11 years

ranging from tiny lesions of a few centimeters¹⁸ to large masses up to 10 cm displacing the entire neck¹⁶, recurrences are generally smaller when they are detected, with the widest known not exceeding the 4 cm¹⁸. Despite the long interval period observed, our case is the smallest recurrence ever reported, along with the 1.5 cm recurrent preauricular tumor of Smith et al.¹⁸.

Only in one case the second tumor was larger than the first one, increasing from 1.5 cm to 2.5 in its greatest dimension¹⁹. Two patients experienced a further recurrence respectively 14 months¹⁶ and 12 months¹⁷ after treatment of the first one. Moreover, Kodet et al. stated that their patient's tumor had undergone a malignant transformation at its second recurrence, due

to histological findings indistinguishable from embryonal rhabdomyosarcoma¹⁷. However, as underlined by the same authors, the tumor was much more likely to have been a well-differentiated embryonal rhabdomyosarcoma, rather than a malignant-evolving fetal rhabdomyoma. All the previously published recurrent cases regarded children less than 9 years old whose primitive and recurring tumors both involved the head and neck region: not only is our study the first of recurrence in an adult patient, but it is also the first one reported beyond the head and neck region. Furthermore, because incomplete excision is considered to be responsible for recurrences, the second lesion usually appeared shortly after the primitive one was removed: only in two cases did the recurrent tumor develop more than 2 years later than the first one, occurring after 5²⁰ and 10 years¹⁸ respectively: hence, another reason why the actual case ought to be considered as unique is the extremely long lasting recurrence interval of 11 years, which is the longest reported.

Grossly, fetal rhabdomyomas are typically small at the time of diagnosis, ranging from 1 to 12.5 cm in their greatest size (median 3 cm), with mucosal lesions bearing a somewhat polypoid appearance. Fetal rhabdomyomas are more often primarily found in the subcutis or submucosa than in muscle, commonly being superficial tumors: this is a useful hint in distinguishing them from rhabdomyosarcomas, along with atypia and mitotic figures¹. Although fetal rhabdomyomas are quite uncommon, pathologists should always be aware of them because they can closely resemble embryonal and spindle cell rhabdomyosarcomas, which undoubtedly represent their main histological differential diagnosis. However, a thorough histological examination and several morphological hints can be extremely helpful in assessing the correct diagnosis in the most challenging cases: firstly, fetal rhabdomyomas usually show pushing margins and are superficially located (dermis and subcutaneous tissue), unlike the infiltrative margins and deep location (intramuscular) that characterize rhabdomyosarcomas; secondly, despite mild cellularity, pleomorphism and mitotic activity do not rule out the diagnosis of fetal rhabdomyomas, marked cellular atypia and pleomorphism, atypical mitosis and necrotic areas are never seen in fetal rhabdomyomas and, therefore, when such features are found a diagnosis of rhabdomyosarcoma ought seriously to be taken into account. Infantile fibromatosis can also resemble fetal rhabdomyomas, especially when the proliferating fibroblasts entrap the contiguous muscle fibers: however, infantile fibromatosis generally shows an infiltrative growth pattern and is much deeply located than fetal rhab-

domyomas; furthermore fetal rhabdomyomas lack the fasciculated spindle cell pattern and the interspersed fat cells that are both hallmarks of infantile fibromatosis¹.

Conclusions

In summary, fetal rhabdomyomas are uncommon tumors, showing fetal skeletal muscle-like differentiation features, that almost exclusively involve the head and neck region. Just a very few cases have been acknowledged to arise from other organs and ours is the first one with a primary endobronchial origin. Due to their benign biological behavior, fetal rhabdomyomas usually display an excellent outcome, with few recurrent cases only in incompletely excised neoplasms. Regarding recurrence, the case described herein shows unique characteristics, not found in any of the reports published to date, since: i) it is the first described aside from the head and neck region, ii) it is the first one in an adult and iii) shows the longest interval since the first excision ever reported.

Finally, physicians should always show great concern when dealing with lesions suspicious for fetal rhabdomyomas, as their differential diagnosis with embryonal or spindle rhabdomyosarcomas may sometimes be extremely challenging.

Ethical consideration

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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