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The Juvenile Ribbons-Foetal Type Rhabdomyoma

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Abstract

Foetal rhabdomyoma is an exceptional, benign, heterologous, immature neoplasm demonstrating skeletal muscle differentiation. Foetal rhabdomyoma commonly emerges in infants and young children with a majority of neoplasms appearing beneath <3 years and a median age of disease emergence at 4 years. Majority of neoplasms are discerned within the head and neck or posterior auricular region. Rhabdomyoma is categorized as cardiac or extra-cardiac subtypes. The neoplasm can be discerned incidentally or appear as an asymptomatic tumour mass or represent as a painless nodule. Foetal rhabdomyoma is pauci-cellular and comprised of primitive, spindle-shaped cells admixed with differentiated myoblasts depicting centroidal nuclei, prominent nucleoli and abundant, eosinophilic cytoplasm incorporated with cross striations.

Keywords

Skeletal Muscle; Cardiac; Extra-Cardiac; Neoplasm

Preface

Foetal rhabdomyoma is an exceptional, benign, heterologous, immature neoplasm demonstrating skeletal muscle differentiation. A striated muscle tumefaction, it commonly

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emerges as a distinctive morphological component of extra-cardiac skeletal muscle neoplasms, in addition to adult or genital type of rhabdomyoma. Foetal rhabdomyoma was initially scripted by Dehner et al., in 1972 [1]. Extra-cardiac rhabdomyomas are un-associated with concurrent developmental anomalies or tuberous sclerosis. Foetal type of rhabdomyoma is an exceptional variant, is challenging to discern and mandates adequate distinction from morphologically similar embryonal rhabdomyosarcoma for commencement of appropriate therapy and superior prognostic outcomes.

Disease Characteristics

Benign skeletal muscle tumours are exceptional, are denominated as rhabdomyomas and represent an estimated 2% of skeletal muscle tumours [2]. Foetal rhabdomyoma commonly emerges in infants and young children with a majority of neoplasms appearing beneath < 3 years and a median age of disease emergence at 4 years. An estimated 50% of neoplasms are congenital or appear within the first year of life. The tumefaction is delineated within an age range of 3 years to 58 years. Around <30% of foetal rhabdomyomas are exemplified in adults exceeding >20 years. A male predominance is observed with nearly 75% of incriminated subjects being male [2,3].

Majority of neoplasms are discerned within the head and neck or posterior auricular region, although sites such as cutaneous surfaces, extremities, mediastinum or retroperitoneum are incriminated. Foetal rhabdomyoma is also discerned within the larynx, oropharynx, oral cavity, thigh or urinary bladder [2,3]. Certain foetal rhabdomyomas are associated with nevoid basal cell carcinoma (Gorlin's) syndrome [2]. Foetal rhabdomyoma is associated with genomic mutations of Protein Patched Homolog 1 (PTCH) protein, emerging as inhibitory receptors for sonic hedgehog signalling pathway [2,3].

Disease Pathogenesis

Skeletal muscle arises from myotomes generated from primitive mesodermal tissue. Preliminary stage of muscle development demonstrates miniature, primitive, spindle- shaped mesodermal cells which differentiate into myoblasts. Myoblasts are spherical to elliptical cells with centric nuclei and abundant, eosinophilic cytoplasm impacted with myofibrils. Upon developing, individual myoblasts align and adhere to configure myotubes. On account of longitudinal proliferation, thickening of myofibrils and peripherally situated nuclei, myotubes evolve into muscle fibres which appear within the human embryo at around tenth week of development [3,4]. Classification of rhabdomyoma is contingent to clinical and pathological manifestations and is categorized as cardiac or extra-cardiac subtypes. Extra -cardiac rhabdomyoma is distinct from cardiac variant wherein specific genetic alterations associated

with extra-cardiac rhabdomyoma remain obscure. Extra- cardiac rhabdomyoma is subdivided into adult, foetal and genital subtypes. Exceptional instances of multi-centric rhabdomyoma can indicate a genetic pathogenesis although association of extra- cardiac rhabdomyomas with PTCH gene or pertinent genetic mutations remains unestablished [3,4].

Clinical Elucidation

The neoplasm can be discerned incidentally or appear as an asymptomatic tumour mass. Additionally, tumefaction can represent as a painless nodule or tumefaction at pertinent sites of tumour emergence. Clinically, the neoplasm may be associated site-specific symptoms such as hoarseness, difficulty in respiration or haematuria [3,4].

Histological Elucidation

Macroscopically, the neoplasm can manifest as a soft, polypoidal tumefaction enveloped within a smooth, intact, glistening, superimposed mucosal surface. Grossly, the neoplasm represents as a well circumscribed mass or polyp of magnitude varying from 2 centimetres to 6 centimetres with exceptional instances extending up to 10 centimetres [4,5]. Generally, a solitary, un-encapsulated, grey/white, tan or pink tumefaction arising from soft tissue or mucosa is discerned. Median tumour diameter varies from 3 centimetres to 5 centimetres. Cut surface is glistening and grey/white [4,5]. On fine needle aspiration cytology, spindle-shaped cells and rhabdomyoblasts imbued with abundant, eosinophilic cytoplasm are discerned [5]. Foetal rhabdomyoma is pauci-cellular and comprised of primitive, spindle-shaped cells admixed with differentiated myoblasts depicting centroidal nuclei, prominent nucleoli and abundant, eosinophilic cytoplasm incorporated with cross striations [5,6].

Foetal rhabdomyoma is categorized into immature, myxoid subtype and intermediate, juvenile type. Immature, myxoid subtype is composed of elongated, spindle-shaped cells dispersed within a myxoid stroma. Typically, classic or myxoid variant is pauci-cellular with abundant dissemination of myxoid stroma. Tumour cells demonstrate miniature, spindle-shaped nuclei with fine chromatin and scanty, eosinophilic cytoplasm with bipolar processes. Cross striations are infrequent and challenging to discern [5,6]. Myxoid rhabdomyoma is composed of fascicles of immature, slender, skeletal muscle cells imbued with delicate, cytoplasmic cross striations and thin, tapering, eosinophilic cytoplasmic processes recapitulating myotubules of 7 weeks to 12 weeks of gestation. Additionally, undifferentiated, primitive, spherical to elliptical, spindle-shaped mesenchymal cells are discerned. Tumour cells are circumscribed by a myxoid or fibromyxoid stroma. Skeletal muscle cells demonstrate peripheral maturation with the occurrence of a “pseudo-cambium” layer comprised of plasma cells and lymphocytes, situated beneath mucosal epithelium [5,6]. Intermediate or juvenile subtype is cellular, composed of

numerous differentiated myoblasts and a minimal component of primitive, spindle-shaped or spherical cells delineating divergent skeletal muscle differentiation. The neoplasm is predominantly composed of miniature, spindle-shaped cells incorporated with delicate, tapered, bipolar or unipolar eosinophilic cytoplasm, fine nuclear chromatin and inconspicuous nucleoli [6,7]. Cellular rhabdomyoma is composed of fascicles of skeletal muscle cells configuring parallel bundles or a plexiform pattern. Enveloping stroma is sparse, collagenous or myxoid. Tumour cells demonstrate variable skeletal muscle differentiation ranging from immature cells with a myxoid pattern to ganglion-like rhabdomyoblasts with prominent nucleoli or strap-like cells imbued with abundant, basophilic or eosinophilic cytoplasm and predominant cross striations [6,7].

Skeletal muscle cells may infiltrate and obscure the tumour periphery. Tumour cells are variably incorporated with glycogen- containing vacuoles. Commingled myoblasts demonstrate an abundant, eosinophilic cytoplasm with peripheral cross striations, centric nuclei and prominent nucleoli. Myoblasts appear confined to the edge of the neoplasm. Aforesaid tumour cell and myoblast dissemination exemplifies a gradient of cellular maturation frequently observed in foetal rhabdomyoma [5].

Foetal rhabdomyoma exhibits a component of primitive, spindle-shaped cells imbued with scanty cytoplasm. Myoblasts may be scarce within foetal subtype of rhabdomyoma. Tumour cells are intermingled within an abundant, myxoid stroma with disseminated chronic inflammatory infiltrate [6,7].

Mitotic figures, enhanced tumour cellularity, cellular or nuclear atypia or tumour necrosis are absent.

On ultrastructural examination, hypertrophied Z band material, thick and thin filaments, numerous mitochondria or mitochondria with inclusions are discerned [5,7].

Figure 1: Foetal rhabdomyoma composed of miniature, spindle-shaped cells with scarce cytoplasm and uniform nuclei with commingled myoblasts with abundant, eosinophilic cytoplasm.

Figure 2: Foetal rhabdomyoma delineating strap-like myoblasts with abundant eosinophilic cytoplasm and intermingled miniature, primitive, spindle-shaped cells with regular nuclei.

Figure 3: Foetal rhabdomyoma demonstrating aggregates of miniature tumour cells with spindle-shaped, uniform nuclei and few myoblasts with abundant, eosinophilic cytoplasm.

Figure 4: Foetal rhabdomyoma exhibiting miniature, spindle-shaped and spherical cells with regular nuclei and fine chromatin with few commingled mature rhabdomyoblasts.

Figure 5: Foetal rhabdomyoma depicting clusters of miniature, spindle-shaped cells with minimal cytoplasm, spherical nuclei and inconspicuous nucleoli admixed with few myoblasts with abundant eosinophilic cytoplasm and spindly nuclei.

Figure 6: Foetal rhabdomyoma demonstrating aggregates of miniature spindle-shaped cells interspersed with few strap-like skeletal muscle cells with abundant eosinophilic cytoplasm and cross striations.

Figure 7: Foetal rhabdomyoma demonstrating skeletal muscle fibres with abundant bipolar eosinophilic cytoplasm, cross striations and an admixture of miniature spindle-shaped cells.

Figure 8: Foetal rhabdomyoma immune reactive to desmin.

Immune Histochemical Elucidation

Foetal rhabdomyoma is diffusely, intensely immune reactive to desmin. Spindle-shaped cells and myoblasts are immune reactive to myogenin, myoglobin, Muscle Specific Actin (MSA), Glial Fibrillary Acidic Protein (GFAP) and MyoD1. The neoplasm is immune non-reactive to cytokeratin, S100 protein, Smooth Muscle Actin (SMA), Epithelial Membrane Antigen (EMA), CD68 and CD34 [2,3].

Differential Diagnosis

Foetal rhabdomyoma requires a demarcation from:

- Embryonal type of rhabdomyosarcoma which classically is associated with an aggressive biological behaviour and represents as a rapidly progressive tumour mass. Microscopically, a dense cambium layer of tumour cells is discerned beneath the superimposed epithelial layer. Mitotic activity exceeds >10 per high power fields. Tumour necrosis and severe cytological atypia are commonly observed [6,7]. Botryoid embryonal rhabdomyosarcoma simulates myxoid variant of foetal rhabdomyoma although lesions are deep-seated with a true cambium layer. Cellular and nuclear atypia, significant mitotic activity, tumour cell necrosis, infiltrative tumour perimeter and lack of peripheral cellular maturation is discerned [6,7]
- Spindle cell variant of embryonal rhabdomyosarcoma is identical to cellular variant of foetal rhabdomyoma although is accompanied by cellular and nuclear pleomorphism with tumour necrosis [6,7]
- Skeletal muscle hamartoma demonstrates a significant skeletal muscle component. Lesions appear as triton tumour or cutaneous rhabdomyomatous mesenchymal hamartoma which are exceptionally discerned in young children. Hamartoma is commonly incorporated with neural and/or mature adipose tissue, in addition to skeletal muscle [7,8]
- Neuromuscular hamartoma is composed of nerve fibres and skeletal muscle confined to a singular perimysial sheath. Nerve fibres are immune reactive to S100 protein [7,8]
- Infantile fibromatosis is a deep-seated neoplasm composed of fascicles of spindle-shaped cells along with an absence of cross striations or undifferentiated cells [7,8]

Additionally, foetal rhabdomyoma requires a clinical segregation from conditions such as submucosal cyst, vascular malformation or unspecified benign lesions [9,10].

Therapeutic Options

A comprehensive or simple surgical extermination of the tumefaction is an optimal treatment strategy. Foetal rhabdomyoma is adequately alleviated with comprehensive surgical resection. Prognostic outcomes are excellent following complete surgical eradication. Incomplete surgical excision may be exceptionally associated with tumour reoccurrence. Also, malignant metamorphoses of foetal rhabdomyoma is documented [9,10].

Conclusions

Foetal rhabdomyoma is diffusely and intensely immune reactive to desmin, myogenin, myoglobin, Muscle Specific Actin (MSA), Glial Fibrillary Acidic Protein (GFAP) and MyoD1. Foetal rhabdomyoma requires a segregation from embryonal rhabdomyosarcoma, skeletal muscle hamartoma, neuromuscular hamartoma, infantile fibromatosis, submucosal cyst, vascular malformation or unspecified benign lesions. A comprehensive or simple surgical extermination of the tumefaction is an optimal treatment strategy.

References

1. Dehner LP, Enzinger FM, Font RL. Fetal rhabdomyoma. An analysis of nine cases. *Cancer*. 1972;30(1):160-6.
2. Cai Z, Thomas J, Alava I, Aakash N, Saluja K, Zhu H. Fetal type rhabdomyoma of the soft palate in an adult patient: report of one case and review of the literature. *Head Neck Pathol*. 2019;13(2):182-7.
3. Diociaiuti A, Inserra A, De Vega IF, Rota C, Surrenti T, Giraldo L, et al. Naevoid basal cell carcinoma syndrome in a 22-month-old child presenting with multiple basal cell carcinomas and a fetal rhabdomyoma. *Acta Derm Venereol*. 2015;95(2):243-4.
4. Wang CP, Chang YH, Chang YT. Fetal rhabdomyoma of the right tonsil with polyp-like appearance. *Case Rep Otolaryngol*. 2015;2015:713278.
5. Thompson LD. Ear foetal rhabdomyoma. *Ear Nose and Throat J*. 2017;96(9):358.
6. Walsh SN, Hurt MA. Cutaneous fetal rhabdomyoma: a case report and historical review of the literature. *Am J Surg Pathol*. 2008;32(3):485-91.
7. Pavlicek J, Klaskova E, Kapralova S, Prochazka M, Vrtel R, Gruszka T, et al. Fetal heart rhabdomyomatosis: a single-center experience. *J Matern Foetal Neonatal Med*. 2019:1-7.
8. Pluym ID, Sklansky M, Wu JY, Afshar Y, Holliman K, Devore GR, et al. Fetal cardiac rhabdomyomas treated with maternal sirolimus. *Prenat Diagn*. 2020;40(3):358-64.
9. Yuan SM. Fetal primary cardiac tumors during perinatal period. *Pediatr Neonatol*. 2017;58(3):205-10.
10. Masmejan S, Baud D, Ryan G, Van Mieghem T. Management of fetal tumors. *Best Pract Res Clin Obstet Gynaecol*. 2019;5:107-12.