EUROPEAN OPHTHALMIC PATHOLOGY SOCIETY

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Case number: (pathology lab nr.: H21-7329)

Title Of Case Presentation : **Intraocular undifferentiated pleiomorphic sarcoma**

Clinical History : A 67-year-old male had suffered a penetrating trauma to the eye with a tree branch at age 13. The trauma was treated conservatively and resulted in loss of light perception. Now he presented at the outpatient department because for six months he had noted a hard subconjunctival lesion inferior on the same eye. Recently this was accompanied by a dull pain that varies in time. Ophthalmic evaluation showed a deeply vascularized opaque cornea and firm, cystic subconjunctival lesions. B-scan showed a mass in the anterior chamber. MRI showed an intraocular tumor with retrobulbar extension and involvement of the optic nerve. PET scan did not indicate any systemic tumor. Because increasing pain in the blind eye with a suspected malignancy an exenteration was performed followed by postoperative radiotherapy 33x2 Gy.

Ocular pathology : Orbital exenteration, 4,3x3,5x3,7 cm. The globe showed an external limbal tumor 5 mm. After breadloafing there was an intraocular elastic white colored tumor that extended apparently through multiple scleral channels to the subconjunctiva anteriorly, and intraconal and extraconal orbital fat posteriorly.

Histopathology : The eye was phthisical with extensive intraocular fibrosis and sclerosis accompanied by bone formation. There was an intraocular and extraocular undifferentiated pleiomorphic tumor with a high mitotic index. Although the bulk of the tumor consisted of multiple extraocular lobular masses, there was an impression of primary origin from the choroid with extension through multiple scleral channels anteriorly and posteriorly along the long and short ciliary arteries. The cells were negative for AB and PAS did not show basement membrane like material. Immunostaining was positive for pan keratin and CK7 and negative for TTF1, CK20, CDX2, BerEp4, PSA, p40, PAX8, GATA3, AR, SOX9, SOX10, HMB45, S100 and NSE. NGS 500 gene testing showed a *TP53* p.R248G mutation. Synovial sarcoma X::18 transloc FISH was negative. Methylation profiling (Heidelberg sarcoma methylation classifier v12.2) showed a clustering with pleomorphic undifferentiated sarcoma albeit with a low calibrated score of 0.65. The CNV profile showed extensive chromosomal gains and losses.

Comment : This case presents a presumably intraocular undifferentiated sarcoma that developed in a phthisical eye more than 50 years after trauma. The tumor appeared to have started intraocularly and was documented to extend to the subconjunctiva and orbit along the scleral channels at multiple sites comparable to uveal melanomas. Primary intraocular sarcomas are exceedingly rare and are not included in the current 4th edition nor part of the planned 5th WHO edition of Tumours of the Eye and Orbit.[1] Even primary sarcomas of the orbit are rare representing 1-2% of all orbital soft

tissue tumors.[2] A short Pubmed search identified three reported intraocular sarcoma cases in English literature to date with two synovial sarcomas[3,4] and one mesenchymal chondrosarcoma.[5] These types of sarcomas would have been identified using the methylation profiling in this case.[6] Moreover FISH for the tX::18 proved negative. Metastasis of systemic sarcoma to the eye appeared more common in Pubmed with two leiomyosarcomas[7,8], one alveolar rhabdomyosarcoma[9] and one alveolar soft part sarcoma.[10] It is however conceivable that chronic inflammation and fibrosis may lead to sarcoma formation in phthisical eyes. Post traumatic sarcomas are well documented in cats.[11] They have been associated with traumatic lens rupture and have been proposed to may partly represent dedifferentiated lens epithelial tumors in the feline setting. The positive staining for pankeratin and CK7 may lend support to this theory in the current case; although positive keratin staining in pleiomorphic undifferentiated sarcoma is well described. Negative staining for S100, NSE and PAX8[12] does not lend further support. Lens epithelial tumors have not been documented in humans to date.[13] Shortly after the current case I received an evisceration specimen from another adult with a painful blind eye that also revealed a undifferentiated pleiomorphic sarcoma with a perfect match to the Heidelberg sarcoma methylation classifier. I therefore call for all EOPS members to search their archives for comparable cases and prepare a manuscript to try and delineate the clinicopathological features of this hitherto underreported diagnosis.

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