Hepatic angiosarcoma

Hepatic angiosarcoma (HAS) is an aggressive mesenchymal malignancy that remains underexplored in its etiology and mutational landscapes. To clarify the association between HAS and end-stage end-stage renal disease (ESRD), Huang et al. exploited nationwide data from the National Health Insurance Research Database (NHIRD) in Taiwan, covering ~99% of the population, from 2001 to 2016. To investigate molecular signatures, they performed whole-exome sequencing (WES) in 27 surgical specimens, including 9 ESRD-associated cases. The NHIRD analysis demonstrated that HAS ranked 2nd among all angiosarcomas in Taiwan, with the incidence rates of HAS being 0.08, 2.49, and 5.71 per 100,000 person-years in the general population, chronic kidney disease (CKD), and ESRD patients, respectively. The standardized incidence ratios of HAS in CKD and ESRD patients were 29.99 and 68.77, respectively. In comparison with nonhepatic angiosarcoma, the multivariate regression analysis of our institutional cohort validated CKD/ESRD as an independent risk factor for HAS (odds ratio: 9.521, 95% confidence interval: 2.995-30.261, $P < 0.001$). WES identified a high tumor mutation burden (TMB; median: 8.66 variants per megabase) and dominant A:T-to-T:A transversion in HAS with frequent TP53 (81%) and ATRX (41%) mutations, KDR amplifications/gains (56%), and CDKN2A/B deletions (48%). Notably, ESRD-associated HAS had a significantly higher TMB (17.62 variants per megabase, $P = 0.01$) and enriched mutational signatures of aristolochic acid exposure (COSMIC SBS22, $P < 0.001$). In summary, a significant proportion of HAS in Taiwan is associated with ESRD and harbors a distinctive mutational signature, which concomitantly links nephrotoxicity and mutagenesis resulting from exposure to aristolochic acid or related compounds. High TMB may support the eligibility for immunotherapy in treating ESRD-associated HAS [1].

A 17-year-old man had pineal region angiosarcoma and a hepatic angiosarcoma. The patient's initial symptom was headache and a CT scan revealed a high-density mass in the pineal region with obstructive hydrocephalus. After the radiation therapy, the tumor disappeared completely on the CT scan. One year later, he developed abdominal pain, and a CT scan and angiogram revealed multiple angioma-like lesions in the liver. The mass in the pineal region showed concomitant regrowth, and finally, the patient died of abdominal hemorrhage. At autopsy, the pineal tumor and hepatic tumor were both angiosarcomas, although it was uncertain which was the original tumor [2].

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Huang SC, Chang IY, Chang CJ, Liu H, Chen KH, Liu TT, Hsieh TY, Chuang HC, Chen CC, Lin IC, Ng KF, Huang HY, Chen TC. Association between hepatic angiosarcoma and end-stage renal disease: nationwide population-based evidence and enriched mutational signature of aristolochic acid exposure. J Pathol. 2023 Feb 23. doi: 10.1002/path.6072. Epub ahead of print. PMID: 36815532.
2)
Seto H, Matsukado Y, Kuratsu J, Takaki S, Tomoda K. [Angiosarcoma of the liver and pineal region]. No Shinkei Geka. 1988 Apr;16(4):409-13. Japanese. PMID: 3386782.