An Overview of 1p36 Deletion Syndrome and Carcinogen Genes; A Role of Genomics in Everyday Medicine

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Background

1p36 deletion syndrome is a relatively common deletion syndrome with an incidence of 1 in 5000 births, making it the most common terminal deletion in humans. 1p36 deletion manifests with an array of phenotypic alterations including, but not limited to, intellectual disability, seizure disorder, dysmorphic facial features, congenital heart defects, and hypothyroidism. According to genetic literature widely available to patients and clinicians, such as ONIN and Gene Reviews, malignancy is not a common manifestation of this syndrome. This case, however, demonstrates malignancy as a consequence of 1p36 deletion syndrome.

Patient Workup

A 24-year-old patient with 1p36 deletion syndrome presented to family medicine with a chief concern of lower back pain. A CT was performed, which showed a burst fracture at his L6 vertebrae. An additional finding of a 13cm mass in his pelvis was noted at that time, prompting further workup.

Imaging

The mass demonstrated hemorrhagic and/or proteinaceous components along with a smooth enhancing 2mm thick septation. The cystic mass seems to extend to the neurovascular bundle in the right gluteal region, most likely leading to the majority of the patients back pain and inability to properly walk. The MRI revealed regional and distant lymphadenopathy with additional spinal lesions.

Genetics

Genomic mapping of the 1p region is ongoing, but it is thought to be home to one or multiple tumor suppressors, which could have played a role in our patient's tumorigenesis. Some of the suspected genetic alterations leading to cancer susceptibility in 1p36 deletion syndrome are CDC2L2, TNFRSF25, AJAP1, TP73, and CAMTA1. Furthermore, when silenced or deleted, CHD5, CAMTA1, KIFIB, CASZ1 and miR034a all have oncogenic properties. Recent studies suggests that a monosomy deletion of the tumor suppressors located in 1p36 is possibly corelated with an increased risk of cancer, but that the classic "two-hit" manner of knocking out the second allele to cause complete loss of the tumor suppressor is not the mechanism behind the cancer development.

Figure 1. (A) Sagittal cut of lower thoracic and lumbar spine showing pathologic fracture at L5 with L5-L6 lytic lesions, indicating metastatic disease . The tumor also extends posteriorly and is causing luminal narrowing of spinal canal. Strikingly, there are many scattered enhancing lesions in pelvis, spine and proximal femur, likely metastasis.

Histology

FNA on the left inguinal lymph node showed poorly differentiated adenocarcinoma with mucinous features. The tissue stained positive for CDX2 and CDX20, indicating the primary mass is likely of GI origin.

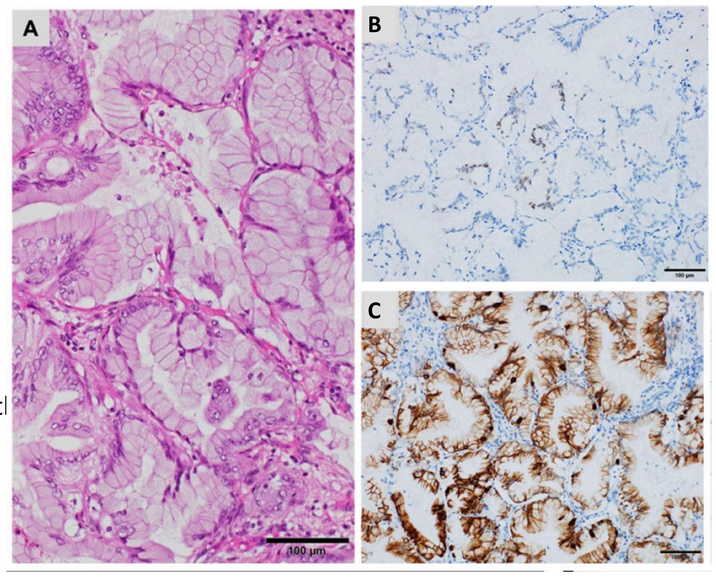

Figure 2. Representative image of a mucinous carcinoma ((A) haematoxylin, eosin and safran) showing (B) a few tumor cells stained for CDX2 and (C) strong staining for CK20 (immunoperoxidase).
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Discussion

Chromosomal microarray will play a pivotal role in analysis of the patients' specific genomic alterations and provide more insight on the tumor's etiology. With molecular medicine providing diagnostic and prognostic information, gaining a strong understanding of the different genetic alterations in syndromes, such as 1p36 deletion syndrome, is vital in all specialties. This case could serve to bring light on a correlation between 1p36 deletion syndrome and an inherent increased risk of malignancy. A strong understanding of how to use molecular medicine in every day patient care improve diagnosis and prognosis, especially in patients with deletion syndromes such as 1p36.

References
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