The role of comprehensive genomic profiling in distinguishing Desmoplastic Melanoma from Malignant Peripheral Nerve Sheath Tumor: Implications for treatment, prognosis, outcomes and delivering patient centered cancer care: Case report and impact on real world outcome.

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Abstract

Desmoplastic Melanoma (DM) are rare variants of melanoma and are frequently confused with soft tissue sarcomas. DM is a variant of spindle cell melanoma typically found on areas of body with chronically sun-damaged cutaneous areas. They can be confused with spindle cell sarcomas.

Malignant peripheral nerve sheath tumors (MPNSTs) are malignancies that demonstrate nerve sheath differentiation in the peripheral nervous system. There are common overlaps between these spindle cell tumors and desmoid melanoma. Genomic origin of both conditions is different and so is the management and treatment. It is very important to differentiate these conditions to ensure appropriate diagnostic work up, optimal treatment choice and outcome. Comprehensive genomic profiling (CGP) can facilitate appropriate diagnostic work up and treatment choice.

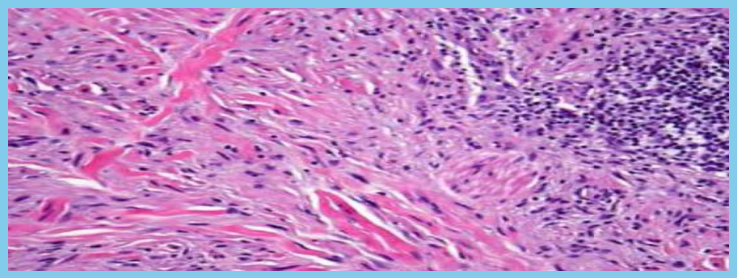
We report a case study of a young Caucasian male with desmoplastic melanoma of lower lip who was initially misdiagnosed as MPNST during the peak of SARS-CoV-19 pandemic. Appropriate look into his Immunohistochemistry (IHC) and subsequent work up including CGP and whole exome sequencing as well as germline testing enabled us to identify definitive diagnosis of desmoplastic melanoma and right type of treatment intervention. Due to the right approach in diagnostic work up, the patient is alive and living life to the fullest for almost four years out now and is in complete response based on MRD assay and imaging studies. Incorporating the latest technology of monitoring his treatment response has enabled him to be one of the rare of the rare cases.

Conclusion

Availability of modern genomic profiling (CGP) and minimal residual disease (MRD) monitoring will likely impact millions of lives across the globe when it becomes standard of care (SOC).

Introduction

Desmoplastic melanoma is a type of spindle cell melanoma. It is more prevalent in male patients than females. It is difficult to identify as it usually lacks pigmentation, commonly resembling benign growth frequently mimicking spindle cell sarcoma. DM is a very rare malignancy. About 1% of all skin cancers are melanomas, and of these melanomas less than 4 percent are desmoplastic melanomas1-3 making DM rare of the rare skin cancer. Due to it's rarity, and frequent resemblance to spindle cell cancers, DM are likely to be confused with other forms of soft tissue cancer. Since the management of both conditions is radically different, appropriate diagnostic work-up is a must to ensure that misdiagnosis does not lead to mismanagement risking life. Malignant peripheral nerve sheath tumors (MPNSTs) are malignancies that show nerve sheath differentiation in the peripheral nervous. These are rare with an incidence of 1.46 per million person-years in the general population4.5. Once again, because of the rarity of these conditions it is mandatory to ensure that full diagnostic work up is carried out to find out and offer the best treatment options. We report a case study of a young 44-year-old Caucasian male with desmoid melanoma of lower lip who was initially diagnosed as MPNST. Despite him being diagnosed at the peak of SARS-CoV-2 pandemic, persistent and meticulous work up including comprehensive genomic profiling, as well as whole exome sequencing and germline testing, we were able to identify true diagnosis and offer appropriate treatment.



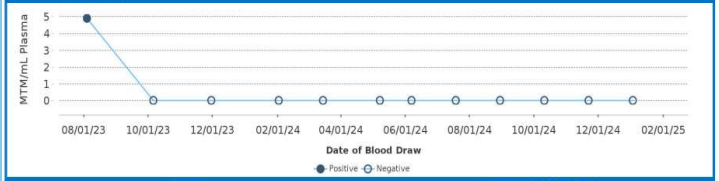
FINAL RESULTS SUMMARY

Signatera Negative

MTM/mL: Not Detected

Mean tumor molecules per mL is calculated based on the mean of ctDNA molecules detected per mL of the patient's plasma. See Limitations section below.

Historical Results



Date	Reported MTM/mL
Jan 03, 2025	0.00
Nov 22, 2024	0.00
Oct 11, 2024	0.00
Aug 30, 2024	0.00
Jul 19, 2024	0.00
Jun 07, 2024	0.00
May 08, 2024	0.00
Mar 15, 2024	0.00
Feb 02, 2024	0.00
Nov 30, 2023	0.00
Oct 06, 2023	0.00
Aug 04, 2023	4.92
Jun 23, 2023	24.93

Discussion

Desmoplastic melanoma (DM) is a variant of spindle cell melanoma. Early diagnosis is typically challenging as it is often amelanotic with mixed dermal components and spindle cell features. There is significant variation in the microscopic appearance of DM which makes it complicated to diagnose with certainly. Spindle cell features can frequently place them in the category of either benign or malignant soft tissue and non-melanocytic spindle cell tumors. Furthermore, some tumors present with a pure desmoplastic invasive component (>90%) while other tumors display mixed features of desmoplastic and non-desmoplastic melanoma. Our patient was originally misdiagnosed as having MPNST precisely due to the same reasons.

Treatment, prognosis and outcomes are completely different in MPNST and DM. Without comprehensive genomic profiling our patient would have received treatment that would not have been effective, and his prognosis would have been gravely impacted. In addition, whole exome sequencing enabled us to identify him to be at a high risk of other disorders too which makes it important to be more proactive than reactive.

Additionally, the availability of MRD6 testing has enabled us to monitor his disease and response at the molecular level and make appropriate adherence to and adjustment to his treatment regimen.

This case illustrates the most important aspect of delivering modern patient centered cancer care that can be individualized to ensure that appropriate treatment decisions are made.

Case Report

A 40-year-old Caucasian male with a history of extensive sun exposure and frequent sunburn on his lips developed swollen lower lips in later part of 2020 after a golf trip. His swelling never fully resolved and had started noticing a palpable lump over lower lip. He sought evaluation and was referred to oral maxilla facial surgeon in the late summer of 2021. He underwent biopsy of the lower lip nodules. His pathology returned as a malignant peripheral nerve sheath tumor (MPNST). He reached out to me for further assessment with a diagnosis of malignant peripheral nerve sheath tumor of the lower lip. His family h/o was positive with SCCA of lips in multiple family members.

Upon full review of his IHC and surface markers, I was not convinced with MPNST as a diagnosis and hence I requested detailed work up including full molecular profiling of his tissue, whole exome sequencing, CGP and Germline testing. In addition, he underwent radical dissection of his lower lip mass and lymph node dissection. His CGP revealed Tumor mutational burden (TMB) is high, MS-Stable, Molecular Markers: ERBB2, ATM, CDKN2A, NF2, TET2, MSH4, BUB1B, and TP53 genes. In addition, he also has Fanconi's syndrome (AR) genes; FANCF. Upon comprehensive review of all findings including examination of entire mass a final diagnosis of desmoid melanoma was made.

After comprehensive work up and review of all imaging studies, he was staged as stage II desmoid melanoma. In view of high-risk features, we offered adjuvant treatment with Ipilimumab and Nivolumab. He stopped after four cycles. He did well for 9 months and then developed an unexplained cough in early 2023. We repeated his imaging studies that revealed left hilar mass. Biopsy confirmed melanoma. He underwent radiotherapy to local area as well as treatment with Opdualag. His repeat scans in summer of 2023 revealed diffuse bony mets in addition to lung mets.

At this stage we started him back on Ipi/Nivo combination therapy. We also carried out MRD assay to measure and monitor mean tumor molecule volume (Figure II). In June 2023, his MTM was 24.93/ml. Within six weeks it dropped to 4.92 in August, and it has been undetectable since then. His scans are also indicative of near CR with some scar tissues. He has been able to live his life to the fullest playing golf frequently as well as traveling and working full time.

References

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