

Clinical Relevance of MDM2 Testing in Lipomatous Tumors of the Extremities

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Objective

Determine the clinical significance of testing for MDM2 gene amplification in Lipomatous tumors of the extremities.

Introduction

Lipomas of the extremities are benign soft tumors of adipocytic origin. Extremity Atypical Lipomatous Tumors or Well-Differentiated Liposarcomas (ALT/LS-WD) are low-grade tumors of adipocytic origin but with a potential of local recurrence¹. Differentiating between lipomas and ALT/LS-WD based on imaging can be difficult. Differentiation often relies on both histological analysis and cytogenetic studies. ALTs are characterized by amplification of the MDM2 gene (12q13-15) and thus cytogenetic MDM2 testing can be a useful tool to establish a diagnosis². However, the question arises whether ubiquitous testing of lipomas and ALT's is necessary and whether this knowledge changes the treatment algorithm for the patient.

Methods

We evaluated patients diagnosed with ALT/LS-WD and Lipoma between 2011 and 2020. Demographic data, tumor location, treatment, and pathology were reviewed.

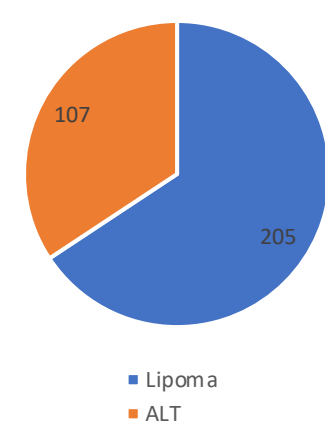


Gross pathology of Lipomatous Tumor³

Results

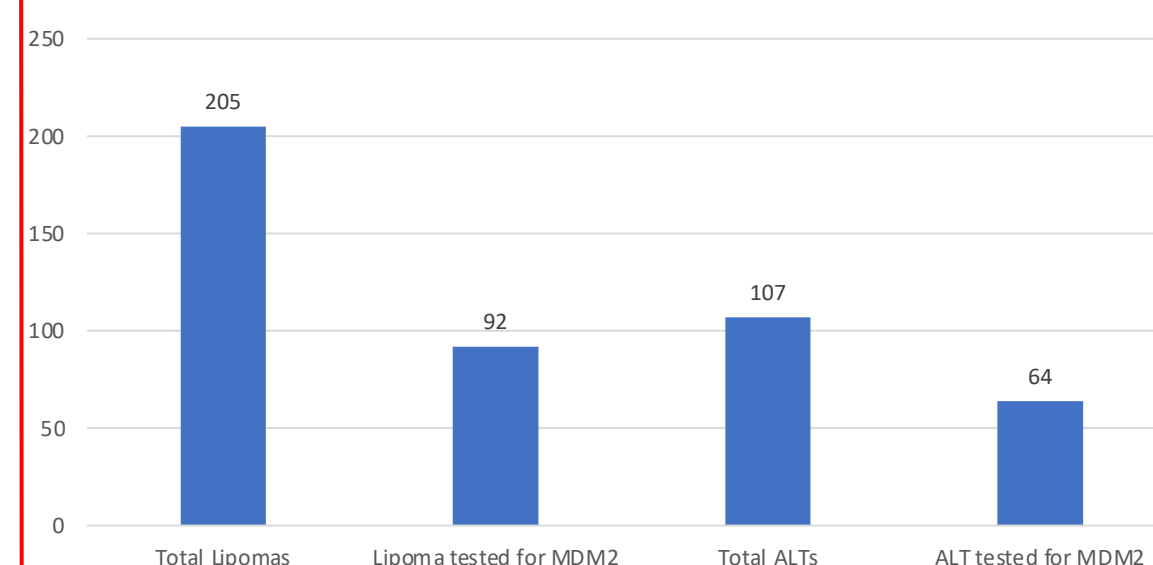
312 patients were identified: 205 lipomas and 107 ALTs. Overall recurrence was 3.9% of patients (n=8) for lipomas and 27.1% of patients (n=29) for ALTs.

Lipomas Vs ALTs Identified



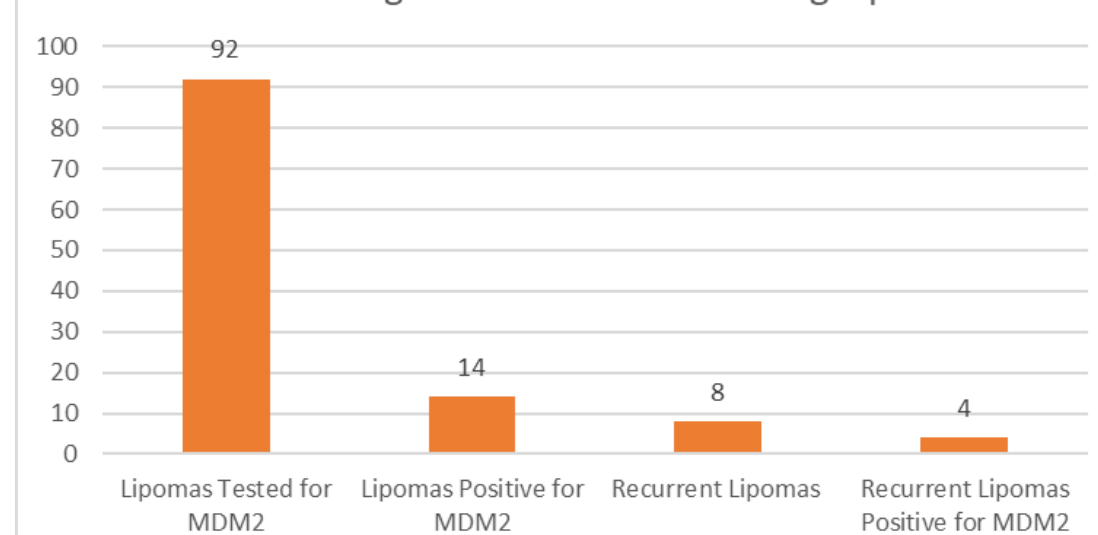
In total 50% of the 312-patient cohort (n=156) were tested for MDM2: of 205 lipomas, 44.87% (n=92) and of the 107 ALTs, 59.8% (n=64).

MDM2 Testing Among Lipomatous Tumors



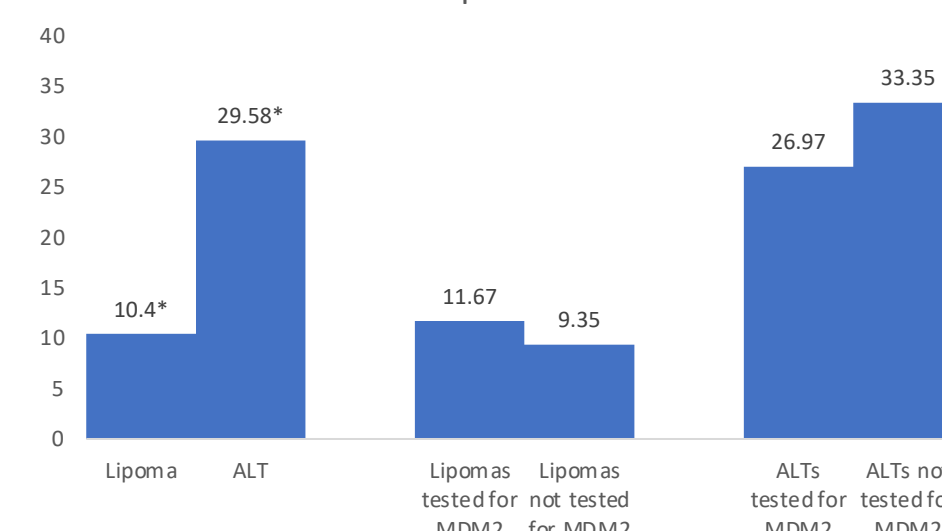
Of the lipomas tested for MDM2, 15.22% (n=14) tested positive, but only 4 of the lipomas that tested positive for MDM2 recurred. Treatment for these 4 recurrent lipomas was surgical excision. Of the 4 recurrent lipomas that were either negative or not tested for MDM2, 2 were treated with surgical excision, 1 was lost to follow-up, and 1 was treated with observation. Treatment of the vast majority of patients who recurred, 91.89% (n=34), was surgical excision.

MDM2 Testing and Recurrences among Lipomas



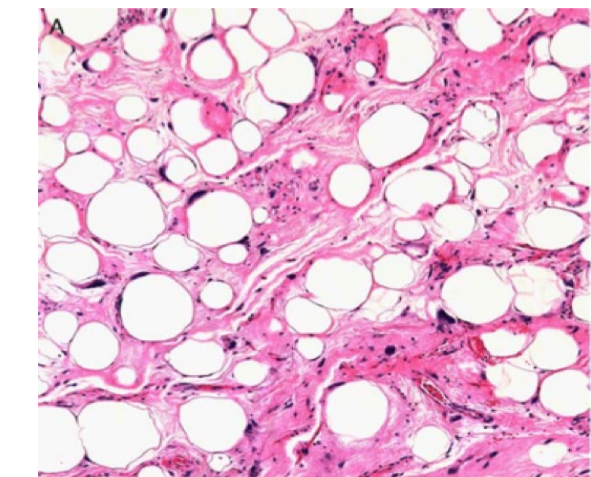
In terms of follow-up, patients from the ALT group had a significantly longer (p<.01) duration of follow-up, after primary surgical excision, than the patients in the lipoma group. The mean duration of follow-up after primary surgical excision for lipomas was 10.4 months, while mean duration of follow-up for ALTs after primary surgical excision was 29.6 months. There was no significant difference between the follow-up duration after primary surgical excision of lipomas tested for MDM2 and lipomas not tested. In addition, there was no significant difference in follow-up duration after primary surgical excision between ALTs tested for MDM2 and ALTs not tested.

Mean Follow-Up Duration in Months

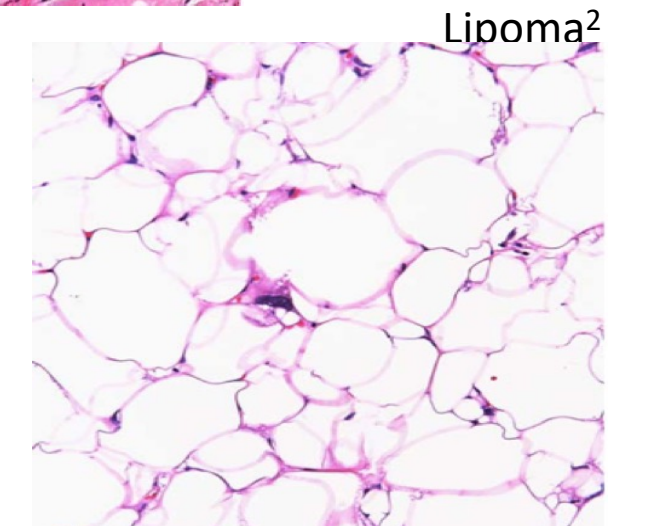


8/205 lipomas recurred, and the mean follow-up was 10.4 months. Time to recurrences was between 24 and 96 months. Of the 8 patients in the lipoma group who recurred, 4 were positive for MDM2, but only 3 lipoma patients were still in follow-up. Mean follow-up for the ALTs was 29.6 months, and 29/107 ALT patients recurred. The time to recurrences was between 12 and 90 months. 20/29 were in current follow-up but only 10 of these were tested and positive for MDM2.

ALT with Equivocal Cytologic Atypia²



Lipoma²



Conclusion

Our results suggest that a more selective approach to using MDM2 testing is warranted. The majority of the Lipomas tested for MDM2 were negative, and of those that came back positive, only 4 resulted in recurrence. While there was a difference in recurrence between lipomas and ALTs, there was no difference in time to recurrence. Treatment of recurrent lipomas/ALTs was surgical excision, whether or not the tumor was positive for MDM2. MDM2 testing is not without financial cost, and in this cohort, testing provided little to no change to the treatment options. Thus, we support the recent recommendations in the literature to limit testing for MDM2 to recurrent lipomas, lipomatous tumors with equivocal cytologic atypia, and deep extremity tumors larger than 10cm in patients over fifty².

References

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