13 Management of locoregionally recurrent melanoma

Locoregionally recurrent melanoma refers to recurrence of melanoma in the anatomical region from the primary site to the regional lymph nodes, after apparently complete excision of primary melanoma. Locoregionally recurrent melanoma has a spectrum of presentations, temporally and anatomically. Anatomically, locoregional recurrence can be defined as:

- local recurrence at the primary excision site, being either:
  - re-growth of incompletely excised primary melanoma, involving the excision site scar or graft (persistent melanoma); or
  - local metastasis at the primary site.
- in-transit metastasis or satellitosis, due to lymphatic and/or haematogenous metastasis
- regional lymph node metastasis
- occurring in isolation or in association with disseminated disease.

These distinctions are important, as the intent of treatment and the prognosis differ greatly. Where possible, patients should be treated in conjunction with a specialist centre.

13.1 Persistent melanoma

The distinction between persistent melanoma and local metastasis is made histologically (see Chapter 7 *Histopathological reporting of cutaneous melanoma*). Persistent melanoma is a rare finding and should be excised completely.[1] There is no evidence indicating the superiority of any particular size of excision margin; margins used for the excision of primary melanoma should be considered. Adjuvant radiation therapy should be considered for close or positive margins unsuitable for re-excision, if normal tissue tolerances can be respected.[2]

Evidence summary	Level	References
Persistent melanoma should be excised completely	IV	1
For persistent melanoma which has been excised with close or positive margins, adjuvant radiation therapy reduces the risk of further recurrence	IV	2

Recommendations

	Grade
1. Persistent melanoma be excised completely	C
2. Adjuvant radiation therapy be considered for close or positive margins unsuitable for re-excision	C

13.2 Local metastasis, in transit metastasis and satellitosis

Local metastasis, in transit metastasis and satellitosis are recurrences that generally occur in the lymphatic vessels more proximally towards the regional lymph nodes. Patients generally have a poor prognosis with frequent development of distant metastasis. The goal of treatment is maintenance of local control. There is a wide spectrum of clinical presentation and rate of disease progression.

Recurrent lesions may be managed by a variety of methods, including excision, cryotherapy, CO_2 laser, intralesional injection or application of drugs or immunomodulating agents, and radiation therapy.[3,4] There is no evidence that other local treatments are equivalent to excision where this is possible. Adjuvant radiation therapy should be considered for close or positive margins unsuitable for re-excision, if normal tissue tolerances can be respected.[2] There is no survival advantage for prophylactic regional drug therapy, although disease free survival is improved.[5] Slowly progressive lesions may be observed until they become symptomatic. There are few data comparing the efficacies of these modalities. These methods are of particular use when the disease progresses slowly.

Evidence summary	Level	References
Adjuvant regional drug therapy improves disease free interval but does not improve overall survival	II	5
For local metastasis, in transit melanoma and satellitosis, a range of local treatments have been reported as effective for local control, with no direct comparison to surgery	IV	3, 4

Recommendations

	Grade
3. Local metastasis, in transit metastases and satellitosis may be managed using a variety of local treatments	C
4. Prophylactic isolated limb perfusion (ILP) is not recommended	A

The management of patients with multiple, rapidly growing or rapidly progressive lesions depends on the anatomical location. Involved limbs should be treated with regional drug therapy. Isolated limb perfusion (ILP) using melphalan under hyperthermic conditions is the standard, but involves a high level of technical skill and experience to minimise complications.[6] Isolated limb infusion (ILI), which is a simpler method of regional drug delivery, appears to provide a response rate and duration of response similar to that of ILP.[7] Response rates approaching 90%, including complete response rates of 60–70%, are routinely achieved with these methods, with low complication rates. Response rates may be sustained for periods approaching a year in approximately 50% of responders. The use of ILP or ILI obviates or delays the need for palliative amputation in most cases. ILI is the more common method in Australia.

Double ILP or ILI procedures are not associated with improved response rates or duration of response. However, further ILP or ILI following relapse is associated with response rates similar to those achieved with the initial ILP.

The use of drugs other than melphalan remains investigational. The addition of tumour necrosis factor α (TNFα) to melphalan does not significantly improve the response rate or duration of response compared with melphalan alone. However, there is some evidence that a second ILP using the combination of melphalan and TNFα may be of value following an initial ILP with a poor response.

Evidence summary	Level	References
Regional drug therapy using isolated limb perfusion (ILP) or isolated limb infusion (ILI) produces high overall, complete and durable responses Repeated ILP or ILI for recurrence in the same limb produce similar response rates to those achieved for the initial procedure ILP/ILI is technically challenging, with a documented incidence of serious complications	II	6, 7
ILI is a simpler alternative to ILP that may produce equivalent results	IV	7

Recommendations

	Grade
5. Recurrence on a limb with multiple or rapidly progressive lesions not suitable for local treatments is best managed with ILP using melphalan under hyperthermic conditions if technically possible	A
6. ILI may be substituted for ILP	C

The management of extensive or rapidly progressive, in transit metastases unsuitable for regional drug therapy (e.g. proximal limb, trunk, head/neck) is difficult and must be individualised and discussed by a multidisciplinary team. Options include combinations of systemic drug therapies and local therapies.[3,4]

Evidence summary	Level	References
For recurrent melanoma with multiple and/or rapidly growing lesions which cannot be managed by regional drug therapy, a range of local treatments have been reported as effective for local control	IV	3, 4

Recommendation

	Grade
7. Recurrence involving multiple or rapidly progressive lesions that are unsuitable for regional drug therapy be managed on an individual basis by a multidisciplinary team proficient in a range of local treatments	C

13.3 Regional lymph nodes

Regional lymph nodes should be considered in the management of locoregionally recurrent melanoma according to the following situations:

- **clinically uninvolved lymph nodes with no previous dissection:** SLNB has been suggested, although evidence for its value in this situation is lacking[8]
- **clinically involved lymph nodes with no previous dissection:** the nodal basin should be dissected, to improve local control.[9] The use of adjuvant postoperative radiation therapy remains controversial and must be decided in relation to its potential toxicity and other therapies. Postoperative radiation therapy could be considered if the pathology report indicates matted nodes, extracapsular spread, and large size and/or large number of involved nodes.[2,10] Although most evidence relates to the initial management of lymph nodes, extrapolation to the recurrent situation seems reasonable. No particular radiation treatment schedule has been found superior to other schedules
- **clinical recurrence in a previously dissected nodal basin:** further dissection should be performed if possible, with consideration of postoperative radiation (if not previously given).[2,10]

Evidence summary	Level	References
For patients without previous lymph node dissection, there is insufficient evidence to determine whether the information provided by SNB following locoregional recurrence of melanoma improves outcome	IV	8
The optimal management of clinically involved lymph nodes in a previously untreated nodal basin is lymph node dissection, which is superior to radiation therapy alone	IV	2, 9
Postoperative radiation therapy to a nodal bed may be effective in reducing the local recurrence rate when there are adverse pathological features	IV	2
The optimal management of recurrence in a previously dissected lymph node region is surgical removal of melanoma, followed by postoperative radiation therapy if this has not been delivered previously	IV	2

Recommendations

In the context of locoregionally recurrent melanoma:	Grade
8. SLNB be considered if the nodal basin has not been dissected and if there is no clinical evidence of nodal involvement	D
9. Lymph node dissection be performed for clinically involved nodes with no previous dissection, following confirmation of melanoma, preferably by fine needle biopsy	C
10. Postoperative adjuvant radiation therapy be considered for adverse pathological findings, though the value remains uncertain	C
11. Clinical recurrence in a previously dissected nodal basin be managed by excision if possible, followed by radiation therapy (unless given previously)	C

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