Raynaud’s phenomenon after radical radiotherapy for tumours of the head and neck

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CASE REPORTS

Endothelial cell injury is implicated in the development of radiation induced tissue damage and may also be involved in the pathophysiology of secondary Raynaud’s phenomenon. Two patients are presented in whom the typical symptoms and signs of Raynaud’s phenomenon developed as a late complication of radical radiotherapy. One had Raynaud’s of the tongue and the other had Raynaud’s of the hands. Both patients had a prior history of primary Raynaud’s phenomenon and in each case the symptoms were repeatedly precipitated by sudden cold exposure. The possible pathogenesis of radiation induced Raynaud’s phenomenon in the head and neck region is discussed.

CASE 1

A 69 year old man presented with a three month history of left sided odynophagia and otalgia. He had a history of primary Raynaud’s phenomenon affecting the hands for about 20 years and asymptomatic aortic incompetence. He was a lifelong non-smoker. At examination under anaesthesia there was a superficial ulcerating lesion in the left oropharynx extending from the tongue base to the lateral aspect of the vallecula. A biopsy of the primary site showed poorly differentiated squamous cell carcinoma. Computed tomography of the neck showed no evidence of lymph node metastases and the disease was staged as T3N0M0.

He was treated with radical radiotherapy using the CHART regimen. The high dose target volume including the tongue base, part of the oral tongue, and the upper deep cervical nodes received a total dose of 56.75 Gy in 36 fractions over 12 days. The dose to elective nodal areas was 37.5 Gy in 25 fractions of 1.5 Gy. The treatment was complicated by a grade 3 acute radiation reaction requiring inpatient admission for analgesia and nasogastric tube feeding. At repeat examination under anaesthesia and biopsy three months after completing radiotherapy there was no clinical evidence of recurrence.

Twenty two months after completing radiotherapy, he developed an uncomfortable tingling in the posterior aspect of the oral tongue after inhaling cold air. This was followed within a few minutes by pain which could be severe if no action was taken to avoid further cold exposure. No other precipitating factors were identified. Investigation by nasendoscopy and magnetic resonance imaging showed no evidence of recurrent tumour. In view of the previous history of primary Raynaud’s phenomenon, he was referred to CMB who confirmed a clinical diagnosis of Raynaud’s phenomenon and in each case the symptoms were repeatedly precipitated by sudden cold exposure. The possible pathogenesis of radiation induced Raynaud’s phenomenon in the head and neck region is discussed.

DISCUSSION

A literature search using Medline has not revealed any previous reports of Raynaud’s phenomenon as a consequence of radiotherapy. Raynaud’s phenomenon affecting the head and neck region is unusual, although it has been described. We believe that this is the first report of Raynaud’s phenomenon occurring secondary to radiotherapy.

Recognised late effects of irradiation include tissue necrosis, fibrosis, and oedema. Much of the late tissue damage after radiotherapy is attributable to vascular injury. The endothelial cell is thought to be a primary target in the mechanism of tissue damage. Morphological changes to the wall of large vessels have been observed after irradiation. Changes to the smooth muscle and adventitia are also observed with the formation of perivascular fibrosis. Over several months endothelial repopulation may occur but the endothelial surface remains irregular and the lumen may become narrowed. Irreversible changes to the microcirculation also occur as evidenced by reduced capillary density in irradiated tissues.

In addition to structural change, the function of the endothelial cell is altered after irradiation. The vascular endothelium is thought to play a part in the relaxation of arterial vessels via the release of nitric oxide and other chemical mediators. Vascular responsiveness is altered acutely after irradiation. Experimental studies show that this is a result of selective impairment of endothelial dependent vasodilation due to decreased nitric oxide synthesis. Chronic impairment of endothelial dependent vasodilation has also recently been demonstrated in vivo in humans.
The typical features of Raynaud’s phenomenon are cold induced pain and numbness of the digits with characteristic triphasic colour change. It may occur as an isolated condition (primary) or associated with an underlying vascular pathology (secondary). The diagnosis is made clinically and there is no specific diagnostic test.

The symptoms are caused by cold induced constriction of small arteries or arterioles with impaired endothelial dependent vasoregulation due to loss of endothelial derived chemical mediators. In addition, tissue hypoxia may increase contractile responses.

The development of Raynaud’s phenomenon of the tongue or lip could be a consequence of late radiation effects on vascular structure (fig 1). The combination of large vessel narrowing and capillary obliteration may cause tissue hypoxia and an increased vascular contractile response. In addition, injury to the vascular endothelial cells by radiation may alter the functional capacity of the endothelium to promote vessel relaxation via chemical mediators. These may result in increased sensitivity of the arterial vascular wall to cold induced contraction.

The two patients described had a history of primary Raynaud’s phenomenon involving the digits, and have developed secondary Raynaud’s phenomenon of the head and neck area.

Learning points

- Raynaud’s phenomenon is caused by cold induced constriction of arteries and arterioles and is exacerbated by tissue hypoxia. Infrequently it may involve the head and neck area.
- Endothelial cell injury and loss of endothelial chemical mediators is implicated in the pathogenesis of Raynaud’s phenomenon.
- Late radiation changes to vessels include arterial narrowing and capillary obliteration which may cause tissue hypoxia. Endothelial cell injury may also occur resulting in impaired endothelial dependant relaxation of the vessel wall.
- The two patients described have a previous history of primary Raynaud’s phenomenon involving the digits, and have developed secondary Raynaud’s phenomenon of the head and neck as a late effect of radiotherapy to this site.
- Raynaud’s phenomenon as a consequence of radiation therapy has not previously been described and we propose that structural and functional changes of the vasculature after radiotherapy are implicated.

REFERENCES