Rare disease

Metastasis of lung adenocarcinoma to the fifth distal phalange of right hand

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Summary

A 46-year-old male was diagnosed of lung adenocarcinoma with right adrenal gland metastasis in January 2009, and underwent chemotherapy (DC (docetaxel and cisplatin) regimen) and stereotactic radiotherapy. In December 2009, whole brain radiotherapy was given to the patient due to brain metastasis. In January 2010, he complained of redness, swelling and tenderness of the fifth terminal phalange of his right hand. Open surgery and biopsy confirmed bone metastasis to the finger. The patient then received local injection of OK-432 combined with radiotherapy. The symptoms were greatly relieved after treatment and the patient has survived for 28 months at the time of this report.

BACKGROUND

Bone metastasis is very common in cancer patients.¹ The reported incidences of bone metastasis of non-small-cell lung cancer (NSCLC) range from 15%–40%.² However, metastasis to the hand bones comprises only 0.1% of the bone metastasis with median survival of about 6 months.³ Here we report a rare case of lung cancer metastasis to the fifth distal phalange of the right hand. Biotherapy in combination with radiation conferred substantial pain relief and a survival of 28 months.

CASE PRESENTATION

A 46-year-old Chinese male smoker was admitted on January 9, 2009 due to progressive non-productive cough and intermittent haemoptysis. Chest and abdomen contrasted CT scan showed a mass in the right lung hilum, a mass in the right adrenal gland and lymphadenopathy in the neck, suggesting lung cancer with right adrenal

gland metastasis. Biopsy of neck lymph node identified adenocarcinoma. Two cycles of DC regimen (docetaxel and cisplatin) were given intravenously to the patient from January to February, 2009, followed by stereotactic radiotherapy in March and April, 2009. Lesion in the neck became smaller, but no change was observed in the lung lesion. The patient did not visit our clinic for follow-up until December 2009, when he developed a severe headache. CT scan revealed multiple metastatic lesions in his brain. He received whole brain radiotherapy starting from 21 December 2009. External beam radiation relieved his headache significantly. In January 2010, he complained of redness, swelling and tenderness of the fifth terminal phalange of his right hand (figure 1). Findings of emission CT (ECT) were not conclusive. He was then treated as paronychia, but symptoms worsened afterwards, especially that severe pain developed. X-ray examination in March 2010, revealed a bone-lytic lesion and swelling of the

Figure 1 Redness, swelling and tenderness of the fifth terminal phalange of right hand (a, b).

Figure 2 X-ray revealed lytic bone lesion and swelling of the surrounding soft tissue (a, b).

Figure 3 Postoperative histopathology of the fifth terminal phalanx of right hand confirmed metastatic adenocarcinoma (a, b 40 $\times$, c, d 100 $\times$).

surrounding soft tissue (figure 2). Open drainage surgery was performed on the patient. Pathology of the biopsy specimen indicated 'inflammatory necrotic tissue and malignant cells'. Immunohistochemical staining suggested 'adenocarcinoma' (figure 3). Symptoms associated with the hand lesion were temporarily relieved but progressively worsened over the following 3 weeks. Then one unit of

OK-432 was injected locally into the hand lesion. Two days later, local skin discolouration was noticed: progressing from red to brown and then to black. Local necrosis was apparent (figure 4). The second dose of OK-432 of one unit was given followed by irradiation (dose of total (DT) 3.0Gy $\times$ 15f, 5f/w 12Mev-E, and DT 2.0Gy $\times$ 5f, 5f/w 6Mev-E). Over the next month, the affected phalange showed

Figure 4 Two days after the injection of OK-432 of one unit. The skin of the surface changed from red to pitchy with apparent collapse (a, b).

Figure 5 Forty days after the injection of OK-432 of one unit. The lesions became necrosis (a, b).

significant atrophy (figures 5 and 6). He is still alive at the time of this report.

OUTCOME AND FOLLOW-UP

The patient is still alive at the time of this report. Follow-up visit is going on by telephone.

DISCUSSION

We report a case of lung adenocarcinoma with metastasis to right adrenal gland and brain, then to the fifth distal phalanx of the right hand, which was managed with combined therapy. The patient has lived for 28 months since initial diagnosis. Bone metastasis occurs at particularly high rates in cancers of the breast, prostate, lung and kidney, accounting for 70% of all patients.¹ The reported incidence of bone metastasis from NSCLC is around 15%–40%, most of which involves spine, rib and pelvis² (figure 7). Metastasis to hand comprises only 0.1% of all osseous metastases.⁴ Low frequency of hand metastasis may be explained by the less red marrow present in hand

bones. When present, distal phalanx is the most common site of metastasis. Incidences of metastasis to the metacarpal, scarpal bones and phalanges are 7%, 17% and 66%, respectively.⁵ Metastasis to the terminal extremities usually manifests as local redness, pain and swelling, and is often misdiagnosed as paronychia, subungual abscess or other benign diseases. Bone ECT is sometimes inconclusive, other radiological techniques, such as x-ray, CT, MRI should be considered. Definitive diagnosis relies on pathology, and probably immunohistochemistry as well.

No effective treatment is available at the moment for bone metastases. Managing such patients, especially those with extremities metastases, always presents a clinical challenge. Common practice is usually palliative. Since these patients usually have very poor prognosis with median survival of only 6 months,⁶ choice of treatments should be made in the best interest of the patients. There is marginal benefit on survival with chemotherapy and radiotherapy is effective in reducing local recurrence and controlling cancer-related pain as well as haemorrhage. Other option includes amputation, which should be considered

Figure 6 Three months after the injection of OK-432 of one unit. The lesions became necrosis and shedding off (a, b).

Figure 7 Anatomic localisation of skeletal metastases from lung cancer is shown.

in case of uncontrollable pain, haemorrhaged or serious infection.^{7–9} Reconstructive surgery is not recommended due to poor prognosis.

In our case, the patient was treated with biotherapy combined with radiation. Prior to the bone metastasis, he had stable disease after chemotherapy and radiation for lung cancer and adrenal metastasis and symptoms related to recent brain metastasis was well-controlled. Since local injection of chemotherapeutic drugs would cause tissue necrosis and difficult-to-heal wounds, we tried biotherapy with OK-432 injection. OK-432 is a penicillin-killed and lyophilised preparation of a low-virulence strain of *Streptococcus pyogenes*.¹⁰ It exerts anticancer effects

by inducing tumour necrosis factor- α , interferon, interleukin-2 and 6, and promoting infiltration of lymphocytes into tumour lesions.¹¹

There are very few reports of local injection of OK-432 in cancer treatment. Based on our limited experience, local injection of OK-432 seems to be safe and effective. When used in combination with radiation, OK-432 could be an optimal option in managing distal extremities metastases. Presumably, OK-432 may increase the efficacy of radiation. However, more research is needed to validate it.

Learning points

- There are three points worth noting in this case.
- (1) To our knowledge, this is the first report of such case in China. There are occasional reports of sporadic cases with similar conditions worldwide. In English literature, there are less than 10 reported cases.
- (2) Metastasis to the distal phalange is frequently misdiagnosed as paronychia, subungual abscess or other benign diseases. Physicians should keep in mind of metastasis in fingers as one of the differential diagnoses.
- (3) As an effective treatment, OK-432, a biotherapeutic reagent could be an option, which may be used in combination with other conventional therapy, such as radiation therapy.

Competing interests None.

Patient consent Obtained.

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