CASE REPORT

Spine and scapular pain: an unusual presentation of colon adenocarcinoma

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SUMMARY

We are presenting an elderly Caucasian woman who was admitted to our hospital for severe lower back pain and scapular pain for 8 days. She had a history of spinal stenosis and we believed this was the aetiology of her pain. However, her pain was not subsiding and hence an MRI spine was performed. It revealed spinal stenosis and abnormal signal in the lower thoracic and lumbar vertebrae. Hence a bone biopsy was performed that came back as metastatic adenocarcinoma. She underwent a bone scan and revealed diffuse disease in thoracic, lumbar, sacral spine as well as third and 10th ribs. Her CT chest/abdomen/pelvis revealed no primary tumour. A mass was detected on her colonoscopy, and pathology revealed adenocarcinoma. She underwent palliative radiation and one cycle of chemotherapy. She was discharged to home hospice care. It is very rare to have osseous metastases as the only manifestation of colon cancer.

BACKGROUND

We believe that this case is important because it highlights an unusual mode of metastatic spread of colon adenocarcinoma. This malignancy more often than not spreads first to the liver or lungs. Osseous spread is rare and by studying the different factors affecting metastasis, we may be able to develop markers on tumour cells to better predict where they are primed to spread to. We know of different chemokines and receptors involved in the pathogenesis of metastasis, but hopefully my case will shed further light on need of more genetic and cellular studies to predict sites of metastasis of certain malignancies. Colon cancer being one of the more common cancers in the world, it would benefit in the future if we could develop targeted therapy towards these chemokines and receptors.

CASE PRESENTATION

In this case report we are presenting an 87-year-old Caucasian woman with a medical history significant for lumbar spinal stenosis and herpes zoster who presented to our hospital with a symptom of worsening back pain for 8 days. The patient had stated that she was having persistent mild back pain for a couple of months; however, over the last 8 days there had been a sudden increase in the severity of her pain. It had initially started in her scapula and then radiated to the middle of her spine. She denied any weakness in her extremities, difficulty ambulation, tingling or numbness in any of her extremities. She was unable to sleep because of her pain. She denied any weight loss, bowel problems,

urinary difficulties or loss of appetite or fatigue. She also denied trauma to the back, nor was she involved in physical activity that may have precipitated her pain.

She suffered from shingles 4 years ago and the rash had started in the scapular area. She has had multiple joint replacements of knees and hips in the past. She used to work as a voice trainee and denied any family history of heart disease, hypertension, diabetes mellitus or any malignancies. She was not a smoker and denied ever abusing alcohol or recreational drugs in the past.

On physical examination she had point tenderness in her thoracolumbar vertebrae (T7 through L5) as well as both scapulas. She had no focal deficits in her muscle strength or sensation. Her knee, ankle, biceps and brachioradialis reflexes were normal. Her rectal tone was normal. Her respiratory examination was unremarkable, while the cardiovascular examination revealed a grade 2/6 ejection systolic murmur, decrescendo type which was best heard in the second intercostal space. There were no skin changes appreciable. Her breast examination was normal as well.

INVESTIGATIONS

The CT chest did not reveal any abnormalities except for a calcified and non-calcified mediastinal and retroperitoneal lymphadenopathy as well as a stable ground glass nodule in the left lower lobe.

The MRI of her cervical and thoracolumbar spine abnormal signals in the lower thoracic as well as the lumbar vertebrae along with degeneration of the lumbar spine as seen in figure 1. A sample of L1 and L2 were taken and was sent for pathology and microbiology. The microbiological workup was

Figure 1 MRI Thoracolumbar spine revealing the abnormal MRI signals suggestive of metastatic bone disease.

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negative for osteomyelitis; however, the pathology report came back as 'Metastatic Adenocarcinoma' which was immunohistochemically positive for CAM5.2, AE1/3, Ber-EP4, EMA and carcinoembryonic antigen (mCEA).

On seeing these results a bone scan was ordered which revealed abnormal uptake in the thoracic spine, lumbar spine, sacrum, pelvis, and third and 10th right ribs.

A CT abdomen with pancreatic protocol was performed which showed no visceral neoplasm or metastases in the abdomen or pelvis.

A colonoscopy and oesophagoduodenoscopy (EGD) was performed with biopsies from a lesion in the ascending colon (figure 2). Pathology from the EGD showed benign cells but the biopsy from the colon revealed poorly differentiated adenocarcinoma of the colon, which was Ki-67 positive. She also underwent a mammogram which revealed no signs of malignancy.

DIFFERENTIAL DIAGNOSIS

Our initial differentials included progression of spinal stenosis of her lumbar spine, progression of degeneration joint disease of her lumbosacral spine, compression fracture and aortic dissection. However, after the MRI was performed we were concerned that she may have a metastatic disease to the bone or osteomyelitis given the abnormal signal that was detected.

The differentials for adenocarcinoma metastases included a primary from the lung, breast, pancreas, ovaries, colon and stomach.

TREATMENT

The patient was initially treated with multiple sessions of radiotherapy to the spine and then followed up with the oncologists. She received one cycle of capecitabine 1000 mg two times a day. She did not tolerate the treatment and was set up with home hospice and pain control.

OUTCOME AND FOLLOW-UP

After initiation of chemotherapy her overall performance status was deteriorating. She suffered from protein malnutrition and developed lower extremity pedal oedema. She was set up with home hospice and unfortunately passed away approximately 5 months after date of diagnosis.

From this case, we conclude that 'back pain' was her initial symptom for metastatic colon cancer and an extensive workup revealed osseous metastases as the first site of metastasis which is a rare mode of spreading for this particular malignancy.

Figure 2 Ascending colon mass which turned out to be the primary tumor.

DISCUSSION

We would like to use this case to talk about osseous spread of colon cancer. Colon cancer is the fourth most common cancer in the USA in the general population; however, it has the third highest incidence rate if we check men and women separately.¹ It is the fourth common cause of death from all cancers regardless of sex.¹ There has been a decline in the mortality rates of colorectal cancer.² The most common sites of distant metastases are the liver, lung and brain, but it can spread to the bone, cutaneous tissue and muscles.³

The sites of spread of carcinomas depend on the primary and each malignancy show organ preferences for spread. There is an interaction of the tumour cells with factors that affect angiogenesis, homeostasis that promote cell growth, survival and invasion and in the end leads to metastases. For example, in breast cancer studies have shown that fibroblasts produced by cancer cells affect the immune system and the cytokines which promote its growth and spread.⁴ In pancreatic adenocarcinoma, the cancer cells produce an upregulating factor which activates toll-like receptor (TLR)-mediated extracellular signal regulated kinase (ERK) signaling to produce the protumorigenic cytokines thereby facilitating tumour growth and escape from innate immune surveillance.⁵ In adenocarcinoma of colon, factors such as laminin 10 and activin A can stimulate epidermal growth factor to activate integrins which promote cell motility and spread of the disease.⁶ Studies have been conducted in rat models to show that site-specific spread does depend on the interactions of the circulating tumour cells and the vessel wall also. In the vessels supplying the liver and the lung there was more cell arrest and probably these sites had more adhesion molecules, while in renal vessels there was less arrest of the circulatory cells. There was rapid extravasation of the tumour cells into the liver and this is considered a rate-limiting step in colon cancer spread.⁷

Most common malignancies to spread to the bone are breast and prostate (50–66%) and the rest of the primaries include mainly lung, thyroid, rectum, bladder and renal cell carcinoma. Bone is a large storage for cytokines and growth factors like tumor growth factor-beta (TGF- β), insulin-like growth factor (IGF), and fibroblast growth factor (FGF) which can promote spread to bone.⁸ Studies in breast cancers have noted that the cytokine RANKL (Receptor Activator of NF-Kappa B ligand) triggers migration of human epithelial cancer cells and melanoma cells to the bones.⁹

As in our case, skeletal metastasis is generally one of the late manifestations of colon cancer. And out of all skeletal metastases only 1.3% arises from the colon.¹⁰ Thus, it can be seen that it is very rare for osseous metastases to be the first site in colon cancer. There are instances where there is resistant spread to the lung, which promotes more bone metastases compared with resistant liver metastases. A retrospective study which involved 252 cases revealed 14 cases with bone metastases but there were no cases which were seen that skipped any organ prior to metastasising to the bone.¹¹ To show the incidence of skeletal metastases without lung or liver involvement would need a much larger study population because of the rarity of such a manifestation. The mortality rate of colon carcinoma spreading to the bones is around 8.1% regardless of direct involvement or lung/liver involvement first.¹¹ Kanthan *et al*¹² performed a 25 year retrospective study and using a local database found 5352 cases of primary colorectal cancer. Skeletal metastases were detected in 6.6% of the cases. Only 1.1% of the cases (60/5352) had only skeletal spread. Lindemann *et al*¹³ studied bone marrow aspirates of patients undergoing resection for colorectal

tumours. They found that patients with tumour cells in their bone marrow had a shorter disease-free survival and had a greater chance of relapsing.¹³

Skeletal metastases are diagnosed with plain radiography, isotope bone scan, CT scans or MRI. Bone scans and MRI have higher specificity.¹⁴ The definitive diagnosis is made from a bone biopsy.

Most skeletal metastases are treated with adequate analgesia, palliative radiation, chemotherapy or surgery if there is evidence of compression fractures.¹⁴ Heras *et al*¹⁵ studied ibandronate in preventing skeletal events in patients with skeletal metastases from colorectal cancers. Their group concluded that administering ibandronate reduced events by 50% compared with the placebo, prolonged the time to first event by 6 months, prolonged time to progression of bone lesions nearly threefold compared with the placebo and reduced skeletal-related mortality.¹⁵ Most of the studies of ibandronate involve breast cancers^{16 17}; however, this could be the first-line medical treatment for osseous metastasis from colorectal tumours.

In conclusion liver and lung are the most common sites of metastases for adenocarcinoma of the lung as these sites have more promoting factors for extravasation of tumour cells. Bone metastasis is uncommon and it is highly unusual for bone to be the first and only site of spread. Our case highlights an uncommon mode of colorectal cancer spread.

Learning points

- ▶ An elderly patient with intractable bone pain without trauma should be suspected for malignancy. Hence age-appropriate screening of cancers must be asked and performed.
- ▶ The most common sites of metastases of colon adenocarcinoma are liver, lung and brain. Bone metastases very rarely occur without the cancer spreading to one of these organs first.
- ▶ There may be chemokines or markers present in cancer cells or host cells predisposing a malignancy to metastasise to a certain location.
- ▶ Growth factors such as fibroblast growth factor, tumour growth factor and insulin-like growth factor as well as receptor activator of nuclear factor-kappa B ligand are all present in bones making it a site for metastases of many tumours such as lung, prostate and breast.
- ▶ Bisphosphonates and denosumab are useful in preventing skeletal related events in patients with osseous metastases. Ibandronate is a medication that may be used more frequently in the coming future.

Contributors CM has helped PP with this case and has made a contribution towards this case.

Competing interests None.

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