A 79 year-old Italian man presents to the Emergency Department with a 4-month history of progressive dysphagia, dysarthria, left-sided hearing loss, diplopia and left facial droop. These symptoms have worsened significantly over the past month, limiting his oral intake to pureed foods and liquids. His speech has also become unintelligible. He denies any fevers, chills, or loss of appetite, but has had increasing fatigue. A review of systems is otherwise negative. Past medical history is significant for tinnitus, affecting his left ear for over 20 years, and occasional joint pain in the legs. There is no history of TB exposure and the patient immigrated to Canada 38 years ago. His medications include meclizine, for dizziness, and clonazepam for sleep.

On examination, the patient is afebrile. Blood pressure, respiratory rate and oxygen saturation are normal. Heart rate is 110, regular and bounding. The head exam is significant for dry mucous membranes and dark pigmentionations on the tongue. The cardiovascular, respiratory, and abdominal examinations are unremarkable. A detailed neurological examination reveals intact mental status and normal function of cranial nerves (CN) I-V. A left-sided CN VI palsy is present. CN VII displays left-sided upper and lower facial weakness as well as right-sided weakness affecting the lower face.

Functions of CN VIII (left), IX and X are also impaired bilaterally. CN XI and XII are intact. Motor examination of the upper & lower extremities reveals normal tone, power (5/5) and reflexes (2+) bilaterally. There is no pronator drift and plantar responses are normal. Sensory examination is normal to touch and proprioception. Tests of coordination and gait are normal.

Laboratory investigations reveal pancytopenia (Hb 80 with MCV 85.2, WBC 3.6, platelets 125), with a leukoerythroblastic blood film. Phosphate is low (0.53) and ALP is high (1,899) with all other electrolytes & liver enzymes normal. Haptoglobin is 2.48, LDH is 1290, and total bilirubin is 10. Serum ACE is normal (19) and serum protein electrophoresis (SPEP) detects trivial gamma spikes.

Brain MRI shows a soft tissue mass in the clivus and petrous bones on the left, extending into the cerebellopontine angle and causing medullary compression. Evidence of diffuse metastatic disease is seen in the skull and cranial vault. Chest and abdominal CT also report sclerotic skeletal metastases as well as co-existent Paget's disease. A right hilar lymph node of borderline size and right iliac lymphadenopathy are noted. Prostate size measures 4.0 cm x 3.5 cm in dimension.

In considering the presence of malignant disease, a bone marrow aspirate and a prostate-specific antigen test (PSA) are obtained. PSA is reported as 200 and bone marrow aspirate shows infiltration by non-haematopoietic malignant cells.

What is the diagnosis?
And the diagnosis is . . .

Case 1

Diagnosis: Metastatic prostate cancer with involvement of clivus and petrous bone.

Discussion

Prostate cancer is the most common male cancer in Canada and the third most common cause of cancer death in men. Due to the widespread use of PSA screening, most men are diagnosed in the early stages of disease, with minimal-to-absent symptoms. Only an estimated 20-30% of patients present with metastatic disease, and one-quarter of them die from their disease within two years.

Metastatic prostate cancer primarily targets bones and lymph nodes, resulting in symptoms such as back pain and leg weakness. Central nervous system complications may also be seen, affecting the spinal cord and the brain. Spinal cord compression is an oncologic emergency, arising from metastases to the vertebral column or paravertebral space. Presenting as back pain, it may also cause muscle weakness, urinary retention or bladder/bowel incontinence. Brain metastases are rare and occurs in the context of failed androgen deprivation therapy for advanced disease. It is rarely seen in the initial presentation of prostate cancer. Leptomeningeal spread represents the most common intracranial pattern, followed by involvement of the cerebrum and lastly, cerebellum. Solitary lesions are more common than multiple lesions.

Common symptoms associated with brain metastases include headache, altered cognition, focal weakness, seizures, and gait ataxia. Cranial nerve involvement is very rare and only a few cases have been reported. One such case is that of a Collet-Sicard syndrome (i.e. paralysis of the lower four cranial nerves) which presents as prostate cancer metastatic to the temporal bone and jugular foramen. Another describes diplopia and a right sixth nerve palsy as the initial features of a prostate cancer mass in the clivus.

Diagnosis of brain metastases relies on a combination of clinical, radiological, and biopsy-guided assessments. Gadolinium-enhanced MRI is invaluable and more sensitive than CT scanning for detection of multiple intracranial lesions. In addition to a PSA level, patients should also be referred for a TRUS-guided prostate biopsy, bone scan, and CT scan of the abdomen and pelvis to look for other areas of metastases.

Both medical and surgical treatments are available for metastatic prostate cancer and focus on reducing circulating androgen levels, chiefly testosterone. The major source of testosterone is the testes, although a small quantity is also produced from the adrenal glands. Androgen deprivation therapy (ADT) may be achieved medically with LHRH agonists such as leuprolide acetate, surgically with bilateral orchectomy, or a combination of both, called maximal androgen blockade (MAB). ADT may cause side effects such as depression, hot flashes, osteoporosis and decreased libido, but avoids the cardiovascular toxicity of estrogens such as diethylstilbestrol (DES), which were used routinely in the 1980's.

ADT is associated with improvements in overall progression-free survival. Current guidelines suggest starting monotherapy (orchietomy or an LHRH agonist) as standard treatment. LHRH agonists appear to be as effective as orchietomy, while causing fewer side effects and maintaining potency. MAB has not shown convincing evidence of improved benefit over monotherapy and should not be routinely offered.

Despite the success of ADT, most men with metastatic prostate cancer will experience cancer progression in an average of 18 to 24 months. They may display biochemical or radiological progression in the form of rising serum PSA levels and the appearance of new metastases. Disease progression, despite ADT, is termed androgen independence. Symptoms at this stage may be debilitating, including bone pain, pathologic fractures, spinal compression, and bone marrow failure, as well as paraneoplastic effects such as weight loss, hypercoagulability, and increased infections. A variety of palliative interventions are available for patients with androgen independence. Docetaxel-based chemotherapy is the only current treatment that carries survival benefits. Other treatments such as mitoxantrone-prednisone-based chemotherapy, bisphosphonates, ketoconazole, and radiotherapy have not demonstrated survival benefit but play an important role in improving quality of life.

Back to the Case

ADT, corticosteroids, and radiotherapy were offered to the patient. There was modest improvement in symptoms with radiotherapy. Hormonal androgen deprivation therapy with bicalutamide and leuprolide resulted in a decrease in PSA from 200 to 54; however, this was not accompanied by a change in clinical disease. Subsequently, palliative care was instituted.

This case illustrates the uncommon occurrence of cranial nerve palsies as a presentation of metastatic prostate cancer. Brain metastasis is rare outside the context of advanced disease and even rarer as a mode of disease presentation. There are only a few cases of cranial nerve involvement, with the current case as the first to report CN VI-X palsies, while sparing the lower two cranial nerves.

References