Metastatic Basal Cell Carcinoma: A Case Report with Pulmonary and Osseous Metastases

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Background

Basal cell carcinoma (BCC) is the most common malignancies worldwide boasting one of the most favorable prognoses due disease tendency to remain local. Yet, clinical presentation with rare distant metastases greatly increases morbidity and mortality (Di Lernia). Due to this combination of rarity and severity of prognosis, it remains difficult yet essential to diagnosis early especially considering the possibility for intervention (Laga). When diagnosed early, most basal cell carcinomas are treated with in office-based therapies varying from topical agents and superficial destruction to more invasive techniques, including surgeries and systemic therapy. These techniques function best with lower stage cancers as no effective therapy exists for locally advanced or metastatic carcinoma (Bichakijan). More recently, emerging molecularly targeted therapies, Vismodegib and Sonedigib, challenge this assertion through demonstrated efficacy among patients with advanced and metastatic basal cell carcinoma (Sekulic, Jacobsen 2016).

Case Report

History of Original Lesion
A 62-year-old white non-Hispanic male was diagnosed in 12/2015 with nodulocystic basal cell carcinoma after 3-year history of progressively enlarging left shoulder mass. Subsequent imaging at time of diagnosis revealed invasion of primary tumor into left lower neck with lymphadenopathy in the left subclavicular space with potential metastases in apical left lung and thoracic spine leading to symptoms of spinal stenosis. Histopathological review of epidermis and dermis and show an atypical basaloid proliferation with peripheral palisading architecture extending into a fibrotic and inflamed dermis (Figure 1). Biopsies of apical lung samples revealed metastases with similar histopathological findings (Figure 2, 3). Tumor cells were positive for CK5, CK6, andP63, but negative for CEA and EMA. Patient was treated with Vismodegib at that time and noted interval improvement in pulmonary and osseous metastatic disease.

Interval History:
11/2017: patient admitted for 1-month history of losing ability to walk. Pt noted improvement after surgical debulking (cervicothoracic decompression, fusion reduction and T2 and T3 laminectomies). Portal bone biopsy confirmed basal cell carcinoma metastasis. Patient at this time completed palliative radiation treatment, and was started on second-line treatment, Sonedigib 200 mg dq.

02/2018-06/2019: Interval imaging noted the patient to have possible slight progression of disease in thoracic spine with stable pulmonary disease.

History of Present Illness:
Patient presented to Vidant Medical Center reports a recent fall. At time of admission, patient denied any bowel or bladder incontinence. He reports no falls in the past 6 weeks but has been stumbling due to increasing leg weakness. Physical exam at admission notable for bilateral lower extremity weakness and tingling. Inpatient MRI showed a tumor compressing the spinal cord. Pt underwent thoracic spine debulking procedures with ability to walk prior to discharge. Pathology confirmed metastatic basal cell carcinoma. Subsequent patient follow-up noted Sonedigib restarted on 10/2019 and mild progression of pulmonary disease CT C/A/P with no new disease or progression in abdomen and vertebrae (01/2020).

Material and Methods

Literature Review was conducted in two phases: 1) 11/14/2019 on PubMed using search terms for "Metastatic" + "Basal Cell Carcinoma" +/- "spine metastases" and "pulmonary metastases" this search yielded 38 articles, which were chosen based on publication in English, available abstract, and available full text article, and 2) inserting these articles into Mendeley app to look for a matching publication, then using the "related document" to find an additional 8 articles. These methods combined to create a total of 16 articles (once filtered for available full text) form which to draw

Punch Biopsy samples were stained using H+E before capturing the histology in the pictures displayed below. Clinical and histopathological findings were summarized below.

Results

Histopathologic Findings: Sections are of epidermis and dermis and disclose an atypical basaloid proliferation with peripheral palisading architecture extending into a fibrotic and inflamed dermis. There is some artifact and tumor necrosis. Tumor cells are positive for CK5/6. Nuclei are positive for P63. Tumor Cells are negative for CEA and EMA (Appropriate controls reviewed). The lesion is transected at the base.

Comment: On balance, this lesion has features of a nodulocystic basal cell carcinoma which has been transected at the base. A complete excision for a full evaluation is recommended. Clinicopathologic correlation is recommended.

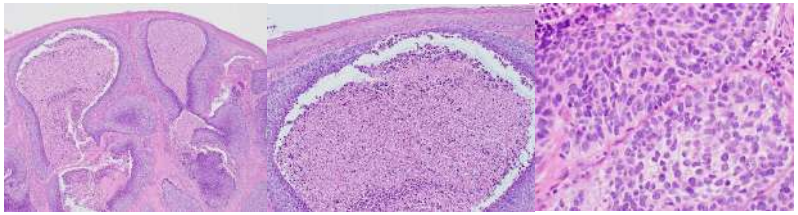

Figure 1 (above): shows successively high magnification of original L shoulder lesion. (40x left, 100x middle, 200x right)

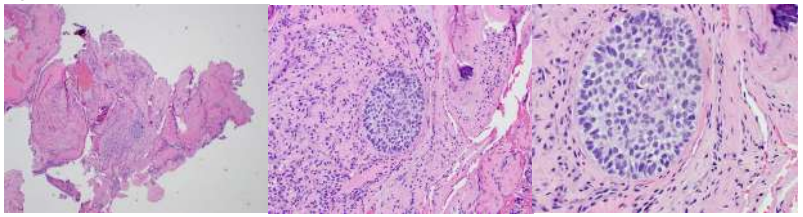

Figure 2 (above): shows successively high magnification of the pulmonary* metastases in our patient. (40x left, 100x middle, 200x right)

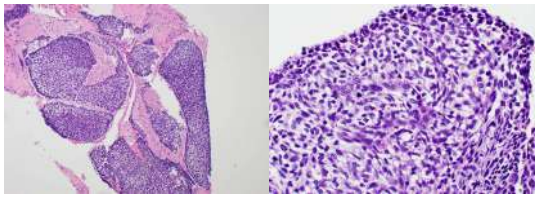

Figure 3 (above): shows successively high magnifications of a secondary pulmonary metastasis (100x left, 200x right)

Characterizing Previous Research [5 6]

Category	Finding
Gender (male-to-female ratio)	2:1
Age of Primary Tumor	45 years
Metastatic Progression Median interval (between onset of tumor and metastasis)	9 Years
Median age (at first sign of metastasis)	59 years
Median Survival (after first sign of metastasis)	8 months-1.6 years (farmer)
Primary Location (Compared to Non-Metastatic)	Similar Primary Tumor Site
Metastasis	Most commonly to lymph nodes, lungs, and bones
Rate of Metastasis	1/1000-1/35000 per case of BCC
Method of Spread	lymphogenic and hematogenic spread equally frequent
Risk Factors	history of persistent BCC for many years refractory to conventional methods of treatment previous radiation treatment either in early adulthood or for localized cancer. (Snow)

- Age and sex unrelated to metastatic spread and survival
- Histologic Degeneration:
  - No histologic evidence for degeneration into SCC
  - Areas of squamous differentiation <15% of metastatic and primary sites
  - Unlikely given histology and pattern of spread

Discussion

- **Takeways**
  - **Our patient matches the previously established norms for metastatic basal cell carcinoma**. By age, sex, and a long and unsupervised history of a primary lesion before presentation with subclavicular lymph node involvement, bone and pulmonary metastases, and subsequent symptomatic spinal stenosis
  - **Our patient displayed a pure basaloid metastasis pathology**. In cases of advanced and metastatic basal cell carcinomas, it is possible to discover evidence of concurrent histopathologic evidence of squamous cell carcinoma. Areas of squamous differentiation in primary lesions are rarely noted, but more likely to metastasize than basaloid subtypes (Domarus).
  - **Our patient has responded well to treatment with Vismodegib and Sonedigib**. Vismodegib was chosen for treatment as first line in this patient's case due to its documented effectiveness. Jacobsen et al 2016 notes Vismodegib superiority in efficacy in treatment of metastatic cases with responsiveness of 34% and complete responsiveness in 4% of cases; By comparison, Sonedigib did not qualify for systemic analysis due to limited evidence.
- **Recommendations**:
  - **The best policy for metastatic BCC is prevention**. Considering the appreciable number of cases of metastatic BCC associated with incomplete excision followed by immediate wound closure (particularly by grafting), it is recommended that wound grafting be delayed for at least six months in order to ensure complete removal (Mikhail).
  - **In localizing metastases, utilize an excellent physical exam**. A good clinical exam to document basal cell carcinoma will include full neurologic, pulmonary, and lymph nodes investigation prior to advanced imaging to assist in localizing metastases.
  - **Small molecule Inhibitors are excellent choices in cases of metastatic basal cell carcinoma.** However, effectiveness in locally advanced cases should be considered in the context of possibility of standard therapies such radiation and surgery.

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