BRIEF REPORT

HISTIOCYTIC SARCOMA: ACUTE ONSET OF WIDESPREAD NODULES AS MAIN PRESENTING SYMPTOM FOR RARE DISEASE

Varintha Baddam, MD[1]; Jasraj Kahlon, MD, PGY-II[1]; Emma Talbott, OMS-IV[2]

[1]Abrazo Health, Goodyear, AZ
[2]A.T. Still University, Kirksville, MO

KEYWORDS

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Osteopathic manipulative medicine

Deep vein thrombosis

Nodules

Shortness of breath

ABSTRACT

Histiocytic sarcoma is a rare and frequently missed diagnosis. With unusual and varied presentations, it typically indicates a rapid patient decline and poor outcomes. The diagnosis requires a high degree of clinical suspicion. In this case, we explore the progression of illness in a 56-year-old white male who initially presented with a 2-week history of soft-tissue nodules scattered throughout his head, neck, torso, and limbs, as well as shortness of breath and knee pain. After a thorough workup including computed tomography imaging of the neck, chest, and lower extremity, as well as a biopsy of a nodule with immunoperoxidase staining, a diagnosis of histiocytic sarcoma was established. Due to the severity of his malignancy, his hospital course was complicated by a deep vein thrombosis. Clinicians should be mindful of the risk of acute decompensation in such cases and can employ the various tenets of osteopathic theory to improve patient quality of life. Depending on the severity of illness, physicians may proceed to facilitate end-of-life measures with grace and dignity.

INTRODUCTION

Histiocytic sarcoma is a malignancy of histiocytes and is an infrequent finding and diagnosis.[1] The disease shows a slight predilection for white males but has a wide and variable age range. A classic finding for patients who present with disseminated disease is extranodal tumors. This presentation, however, has a vast differential diagnosis and can pose a challenge to health care providers. In this case, the patient presented with a rapid onset of widespread disease and was experiencing a fast decline of his overall health. Osteopathic principles and practice were not overtly carried out in the management of this case; however, in retrospect, we can appreciate what these practices could have been, and can consider their applications in future similar scenarios.

CORRESPONDENCE:
Emma Talbott, OMS-IV | sa203677@atsu.edu

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HISTORY, REVIEW OF SYMPTOMS, AND PHYSICAL FINDINGS

A 56-year-old Caucasian male with a medical history of chronic obstructive pulmonary disease (COPD), Chiari malformation with shunt, cellulitis and abscess, and significant tobacco use presented to the emergency department with the chief complaint of widespread nodules that had developed on his abdomen (Figure 1), all four extremities, and face in the previous 2 weeks. This was associated with new-onset shortness of breath, subjective fevers, muscle aches, lethargy, and bilateral knee pain that was worse with ambulation. Family history was significant only for hypertension and primary malignant neoplasm of the lung in the patient's father; the patient lived at home with his niece and denied any new sexual partners, recent travel, sick contacts, and unexplained weight loss. He further denied any associated pain, pruritus, bleeding, crusting, or discharge from the nodules.

At the time of admission, the patient's vitals were notable only for an elevated blood pressure of 154/90 mm Hg. On physical exam, the patient was noted to have a nodule on his upper lip that measured 5 cm in diameter; the surrounding tissue was swollen such that it caused the patient significant dysarthria. Expiratory wheezes were appreciated without the use of accessory muscles.

Multiple quarter-sized soft-tissue nodules were noted on the abdomen, on all four extremities, and especially around the knees bilaterally. No neurologic deficits were appreciated on presentation.

INITIAL DIFFERENTIAL DIAGNOSIS AND INITIAL PLAN

The initial differential diagnosis for this patient was vast, considering the nonspecific and rapid onset of symptoms. Coccidioidomycosis, syphilis, disseminated lung malignancy, cutaneous lymphoma, and advanced HIV infection were considered, investigated, and excluded.

Initial blood tests showed aberrant red cell distribution width (14.9, high), mean platelet values (7.0, low), relative lymphocytes (8.6, low), and absolute lymphocytes (0.8, low). A complete metabolic panel was significant only for an elevated alkaline phosphatase (110). With other values within normal limits, this information was insufficient to make hard conclusions, but pointed towards the possibilities of bone or bone marrow disease, viral infection, or an autoimmune disease.[2]

Initial diagnostic imaging included computed tomography (CT) of the right lower extremity, of the soft tissue of the neck, and of the chest, all without contrast. These imaging modalities revealed widespread disease. The lower-extremity CT showed moderate knee effusion and diffuse soft-tissue nodules within the infrapatellar fat pad and neighboring soft tissues. The neck CT showed left-sided premandibular soft-tissue nodular lesions and projection of the upper lip with a cleft-like deformity, which gave the impression of a possible infiltrative neoplastic lesion. No evidence of airway compression was observed. The chest CT was negative for evidence of mediastinal hilar widening, pleural effusion, pneumothorax, or lymphadenopathy. It did however show 1.2-cm and 0.9-cm ground-glass nodules in the right upper lung, which suggested either a pneumonia-type disease or a pulmonary metastatic process. The CT further revealed a 2.8x2.6-cm soft-tissue nodule in the extrapleural left chest wall, which raised further concerns for metastasis. In the upper abdomen, a 1.1-cm perirenal nodule was also appreciated.

In light of these findings, hematology-oncology specialists and infectious disease specialists were consulted, and a nodule biopsy was obtained from the patient's right shoulder by interventional radiology.

FINAL DIAGNOSIS AND INTERVENTION WITH OSTEOPATHIC CONSIDERATIONS

Histiocytic sarcoma is uncommon in humans, but more than that, it has a tendency towards irregular presentations across multiple organ systems and even imitates other disease processes.[3] The diagnosis therefore requires pathology studies, as it is important to rule out other suspected neoplasms before assigning histiocytic sarcoma. Microscopic examination may disclose "large tumor cells with variable pleomorphism but often resembling mature histiocytes," and malignant cells often invade lymphatic organs like the spleen and lymph nodes.[4] Tumors are prone to necrosis, and display "increased mitotic figures and apoptotic cells."[4] A study by Janke and Rehg on mouse histiocytic sarcoma revealed that in 80% of cases, both spindle cells and small round cells commonly present even within the same tissue specimen.[3] (Mice were utilized because they, in contrast to humans, have a high incidence of the disease and generate more samples for analysis.) Cells in histiocytic sarcoma can organize into discrete nodules, diffuse sheets, or sometimes both, and lymphocytes were variably found interspersed among the malignant cells. Diagnosis requires immunohistochemistry staining (IHC) positive for CD68, CD163, and lysozyme.[4] Other positive markers are possible in the diagnosis. Stains that indicate a negative diagnosis include "T-cell, B-cell and follicular dendritic cell markers" (CD21, CD23, CD35) and Langerhans cell markers (CD1a and CD207).[4,5]

Following our patient's tissue biopsy, surgical pathology reports and microscopic examination showed malignant cells. Specifically, "diffuse lymphoid proliferation composed of medium to large lymphoid cells with vesicular nuclei and small distinct nucleoli [with] single-cell necrosis" was noted throughout the specimens. Immunoperoxidase stains were strongly positive for CD4, CD43, CD56, CD68, CD163, Factor XIIIa (weak), Ki-67, and lysozyme. Given these findings, the patient was assigned a diagnosis of histiocytic sarcoma.

Considering the advanced nature of the patient's disease, he was immediately started on an aggressive inpatient therapeutic regimen that included cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone (CHOP). It was also deemed appropriate to schedule an immediate transfer of the patient to a specialized facility to begin chemotherapy.

Osteopathic Considerations

Recalling the five osteopathic models (including the structural, respiratory-circulatory, metabolic, neurologic, and behavioral models) can provide a useful guide in treating the patient as a whole person.[6] In this case, the structural and respiratory-circulatory models were overall contraindicated due to the malignant nature of the patient's disease. However, following the neurologic model, he would likely have exhibited several Chapman's points, given his multiple-organ involvement. Consider: possible scattered points in the clavicular region corresponding to the masses found on the patient's upper lip and soft-tissue neck regions (assuming associated visceral involvement); right anterior ribs 3 and 4 at the sternocostal junction, corresponding to the right upper lung segment; 1 cm superior and lateral to the umbilicus, corresponding to the perirenal mass.[7] Concerning counterstrain, the patient's bilateral knees would likely have had some point tenderness. Treating Chapman's points and counterstrain points is a simple and low-risk method of pain relief. Furthermore, in patients with terminal illness, the behavioral model, which aims to optimize a patient's psychological and spiritual health, can be particularly beneficial.[6] Facilitating consults with psychologists and social workers, visits from hospital chaplains, and time spent with family are intended to help a patient cope with any stress and depression, and generally guide the patient through such a challenging personal time.

FOLLOW-UP AND OUTCOMES

Unexpected events in this patient's case were limited to his short hospital stay. However, on his second day of stay, a deep vein thrombosis (DVT) was discovered. The patient complained of newly increased pain and edema in his right calf. On physical examination, his skin was warm to the touch and without discoloration. A venous duplex ultrasound revealed a completely occlusive venous thrombosis in the right posterior tibial vein, which was subsequently treated with full-dose Lovenox. The patient was also encouraged to ambulate frequently.

The patient was lost to further follow-up after transfer to the specialized facility.

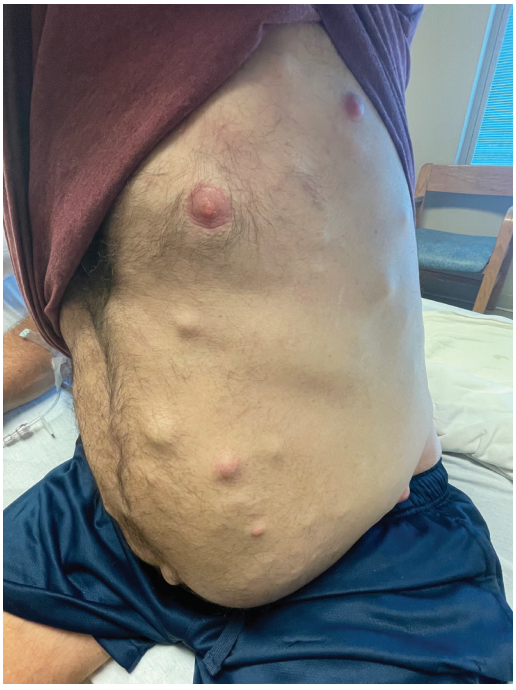
DISCUSSION

Histiocytic sarcoma is a rare and easily missed diagnosis that is typically indicative of rapid patient decline and poor outcomes. In this case, we discussed a 56-year-old white male who presented with a 2-week history of widespread soft-tissue nodules, shortness of breath, and knee pain. Diagnosis of histiocytic sarcoma was established obtaining a biopsy sample of the nodule and performing immunoperoxidase staining.

The rarity of this disease makes it somewhat sparsely covered in the literature, and data providing appropriate treatment modality are limited.[8] Presenting symptoms can vary from widespread extranodal disease to even the involvement of one singular lymph node.[9] Some evidence indicates that the size of presenting tumors may affect outcomes.[10] Our case agrees with the literature in that the presentation of the patient and the course of his disease were severe in both timing and progression up to presentation.

FIGURE 1:

Soft-tissue nodules on abdomen.



Unfortunately, losing this patient to follow-up meant that his disease evolution and ultimate outcomes cannot be considered. Literature indicates overall survival with a diagnosis of histiocytic sarcoma is short. One study showed that out of a cohort of 158 patients, the average overall survival after diagnosis was 6 months.[11] With this in mind, having a suspicion of histiocytic sarcoma is important in the face of characteristic patient presentation to be able to correctly and promptly diagnose it, thereby affording patients the most time to seek specialized treatment.

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