CASE REPORT

Primary granulocytic sarcoma presenting as an external auditory canal mass in a newborn with a draining ear

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1. Introduction

The differential diagnosis of pediatric neoplasms in the external auditory canal (EAC) and temporal bone is challenging. Complex diagnoses such as...
rhabdomyosarcoma, lymphoma, and Langerhans’ cell histiocytosis (formerly known as Histiocytosis X, and its related pathologies such as eosinophilic granuloma, Letterer-Siwe, and Hand-Schuller Christian Disease) may represent some leading concerns. Ultimately, it is a combination of clinical, radiographic, histological, and immunohistochemical means to make a diagnosis.

Granulocytic sarcomas (also called myeloblastomas or chloromas) are solid, extramedullary collections of myeloblasts occurring anywhere in the body [1,2]. The entity was first described in 1811, but the association with leukemia was not identified until the late 1800s [3]. This pathology is commonly associated with acute myelogenous leukemia (AML), and less typically with acute lymphocytic leukemia (ALL), myeloproliferative and myelodysplastic syndromes such as hypereosinophilic myelofibrosis, polycythemia vera, and myeloid metaplasia in adults [4].

The term chloroma, derived from the Greek chloros, is secondary to the presence of myeloperoxidase within the myeloblasts giving the tumor a variably greenish hue upon sectioning [1,3,4]. Histologically, especially in the case of no pre-existing hematologic disorder suggesting a myeloid origin, the diagnosis is difficult. Incorrect initial diagnosis rates of primary granulocytic sarcomas are reported to be from 47 to 100% [5,6]. Granulocytic sarcomas are most commonly mistaken for non-Hodgkin’s lymphoma (diffuse large cell type), soft tissue sarcomas, Ewing’s sarcomas, or poorly differentiated epithelial tumors.

2. Case presentation

A term fraternal twin male (twin A) was born via uneventful vaginal delivery. His hospital course was uncomplicated, including a normal hearing screen, and was discharged home with his sister on day of life (DOL) 3. On DOL 5, the infant was noted to have right otorrhea which the parents regarded as cerumen. On DOL 14 the infant was taken to an outside emergency department when the otorrhea was noted to be increasingly purulent and was treated with amoxicillin. Cultures returned *Staphylococcus aureus*. The otorrhea persisted and, on DOL 21, his antibiotic regimen was changed to amoxicillin/clavulanic acid and ciprofloxacin/dexamethasone otic suspension. The infant was subsequently seen by pediatric otolaryngology with the finding of significant swelling of his external auditory canal (EAC) and a flat tympanogram. Examination under anesthesia demonstrated a friable polypoid mass in the EAC. Biopsies were taken and a surgical foam wick placed for stenting. The tympanic membrane (TM) could not be visualized. Computerized tomography (CT) of the temporal bones showed near total opacification of the EAC and middle ear cavity. The ossicles, bony labyrinth, and internal auditory canal were unremarkable. There were no lytic lesions on plain films. Infectious disease and hematology/oncology were consulted. Due to neutropenia, a bone marrow aspirate was done to rule out congenital neutropenia. This demonstrated a normal bone marrow aspirate with sequential maturation and no evidence of malignancy. The neutropenia was attributed to infectious etiology or drug effect such as nafcillin. The biopsy demonstrated atypical histiocytic infiltrate consistent with monoblastic sarcoma, M5 AML type. This was supported by immunohistochemical staining which was positive for lysozyme and CD68. Stains were negative for S-100, desmin, mast cell markers and tryptase. Electronic microscopy (EM) was negative for birbeck granules. Karyotyping showed normal male. Neutrophil counts increased with G-CSF (granulocyte colony stimulating factor).

He was treated with chemotherapy per Children’s Oncology Group protocol AAML02P1, a pilot study for the treatment of children with AML. He was given five courses of chemotherapy given every 28 days. This consisted of the following: induction 1-cytarabine, daunorubicin, etoposide; induction 2-cytarabine, daunorubicin, etoposide; intensification 1-high dose cytarabine, etoposide; intensification 2-mitoxantrone, cytarabine; and intensification 3-cytarabine, asparaginase. He tolerated therapy well with no significant complication except for an episode of neutropenic fever and coagulase negative staphylococcal line infection.

He has been off therapy for 2 years. Bone marrow done at he end of treatment and serial CT scans showed no evidence of disease. Subsequently, he has had a tube placed in the left ear and has a residual perforation on the right with a normal-appearing middle ear.

3. Discussion

Primary granulocytic sarcomas or chloromas may be a harbinger of acute myelogenous leukemia, specifically, AML subtypes M1 and M2 in adults, and in infants, M4 and M5 [2,4,7]. The delay between initial presentation as a primary granulocytic sarcoma and disease manifestation of AML is usually months but can be years. Less common in pediatrics, granulocytic sarcoma development may also be indicative of relapse if there is a history of myeloproliferative disorders or of subsequent blast crisis after CML diagnosis [1].
Granulocytic sarcomas are associated with multiple chromosome abnormalities such as t(8;21) and inv(16) and rare monosomy, as well as focal expression of surface markers, CD 56, 2, 4, and 7 \[4,7\]. Leukemia associated with t(8;21) has been described as having favorable remission rates. In the presence of granulocytic sarcoma formation, however, complete remission rates are decreased from 92 to 50\% \[8\]. When granulocytic sarcomas occur in bone, myeloblasts are thought to travel from the marrow through the haversian system to rest in the periostium, and there is a propensity for ligamentous involvement. Symptoms are the result of tumor mass effect and are related to tumor location ranging from indolent to painful swellings. In the head and neck, their symptoms may range from hearing loss to pain \[3,4,9\]. Facial nerve palsy can be the result from pathology located at the cerebellar pontine angle, temporal bone, or parotid.

Staining for chloroacetate esterase, myeloperoxidase, lysozyme, CD 43, 68, and 34 may assist in determining the diagnosis or expedite timely and accurate therapy \[7,10,11\]. CD 68, myeloperoxidase, chloroacetate esterase and lysozyme are used as generalized markers for granulocytes. CD 34 is an immature blast marker. CD68 and lysozyme, both monocytic antigens, were positive (Figs. 1 and 2) yielding a diagnosis of monoblastic sarcoma. S-100, negative in our current patient, may be used to rule out certain neural tumors and melanoma. Desmin is used to identify rhabdomyosarcoma; trypase and mast cell marker stains suggest certain lymphomas. Electron microscopy for birbeck granules indicates langerhans’ cell histiocytosis which was also negative in our young patient.

Granulocytic sarcoma as a prognostic indicator must be correlated with the clinical picture. Typically, primary granulocytic sarcomas are prognostically poor. As the sole presenting feature of acute myelogenous leukemia, the prognosis is favorable compared to those with synchronous medullary or circulatory involvement or those in remission at the time of presentation \[12\]. It is generally viewed as a negative prognostic indicator if associated with relapse as well as having a poorer treatment response with a mean survival of 20–22 months \[1,7,13\]. In such a situation, it is clearly not an independent prognostic factor but confounds an already unfortunate clinical picture.

Incidence in the head and neck is quoted at 12–48\% of all granulocytic sarcomas, with most sources consistently referencing an incidence <20\% \[14,15\]. They most commonly present in the orbit and nasopharyx. It is seen in approximately 3–5\% of pediatric patients with acute myelogenous leukemia with a slightly lower incidence within the general population with equal prevalence in both sexes \[3\]. Orbital involvement seems to have a 3:2 predilection for boys \[16,17\].

Radiographically seen as lytic lesions, CT scans show a well-defined area of increased attenuation with a peripheral zone of enhancement. On MRI, myeloblastomas have signal intensities similar to those of marrow on T1 and T2 images and enhance with contrast, thus making it impossible to distinguish it from meningiomas or lymphomas \[4,18\]. The current patient was found to have an opacified EAC and middle ear (Figs. 3 and 4) prior to diagnosis. Following therapy, a follow-up CT scan was obtained with complete resolution of external and middle ear findings.

There is no role for surgery beyond biopsy, and rapid diagnosis is imperative to successful treatment as early chemotherapy has been successful in inducing complete remission. Radiation therapy has not been shown to be helpful with primary

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**Fig. 1** Immunohistochemical staining with anti-CD68 was positive in the atypical histiocytic infiltrative cells.

**Fig. 2** The atypical histiocytic cells stained positive for lysozyme.
granulocytic sarcomas. It has been demonstrated that resection and/or radiation may benefit local control but not influence overall survival. [19] Radiation, however, may be helpful in the event of relapse, especially when relapse occurs during chemotherapy [12]. Treatment of the disease process is specific to the tumor. For example, if the granulocytic sarcoma is histologically and immunohistochemically associated with a specific subtype of leukemia, that patient is treated with the appropriate chemotherapeutic regimen for that subtype.

When chemotherapy was administered, the probability of developing leukemia was decreased from 71 to 41% [19].

4. Conclusion

Granulocytic sarcomas, also called myeloblastomas or chloromas, are solid, extramedullary collections of myeloblasts that may be found anywhere in the body. Granulocytic sarcomas should be suspected in cases of temporal bone tumors, even in the absence of systemic manifestations of leukemia at any age. Recognition of this rare entity is important because early aggressive chemotherapy can bring about regression of the tumor and improve survival. There is one report of a lymphoma recurrence in an adult female in the nasopharynx, external auditory meatus, and bone marrow [20]. No previous report was found involving newborns or presenting with an isolated EAC mass without bone marrow or circulatory involvement.

References

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