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Egg Shell Nodal Calcification in a Patient with Sinus Histiocytosis with Massive Lymphadenopathy Treated with Interferon

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Summary: CT showed egg shell calcification in the cervical lymph nodes in a patient with sinus histiocytosis with massive lymphadenopathy treated for 1 year with interferon. CT scans before interferon treatment had shown no nodal calcification.

Index terms: Neck, computed tomography; Rosai-Dorfman disease; Histiocytosis; Drugs

Cervical lymph node calcification is uncommon, having been reported in tuberculosis, histoplasmosis, seminoma, lymphoma, sarcoidosis, and *Pneumocystis carinii* infection (1–9). Cervical nodal calcifications also have been described after BCG vaccination and in patients with lymphoma after radiation therapy and/or chemotherapy (10–13). The pattern of calcification of cervical lymph nodes, when it does occur, is typically irregular and not in an egg shell pattern.

In the mediastinum, the imaging appearance of nodal egg shell calcification is classically associated with silicosis. However, it also has been reported in sarcoidosis, progressive scleroderma, and tuberculosis (14–22). Non-nodal egg shell-type calcification also has been reported in lesions of pheochromocytoma, parathyroid adenoma, and thyroid carcinoma (23–26). The purpose of this paper is to present a patient with sinus histiocytosis with massive lymphadenopathy, in whom egg shell calcification of several cervical lymph nodes developed after treatment with interferon.

Case Report

The patient is a 19-year-old man diagnosed as having sinus histiocytosis with massive lymphadenopathy with a 7-year history of disease. Initial diagnosis was made by biopsy of one of the enlarged cervical lymph nodes. Histologic exam demonstrated a polymorphous cellular infil-

trate, with histiocytes predominating. The histiocytes exhibited foamy eosinophilic cytoplasm and were positive for S-100 on immunohistochemical staining; typical findings in sinus histiocytosis with massive lymphadenopathy. Because the lymphadenopathy had caused tracheal and esophageal compression, he had required a tracheostomy tube and had become cachectic. During the first 5 years of his illness, he had been seen by multiple physicians and received both conventional medical therapy such as steroids and alkylating agents, and homeopathic therapy including intravenous treatments and chelation therapy. About 2 years ago, the patient was not thriving and was unwilling to take further chemotherapy. He began interferon therapy, initially 3 million U per day, and subsequently 6 million U per day. Over the next several months, the adenopathy receded, the tracheostomy was removed, and he had gained 15 pounds. The interferon therapy was continued for a total of 1 year, at which time he had gained a total of 52 pounds, his adenopathy was reduced by about 90% by volume, and he was able to engage in some athletics in school. Because he stabilized at these levels, the interferon therapy was discontinued. He remained stable for about 10 months. However, in the past 2 months, his adenopathy started to increase in size, again causing some respiratory compromise. Computed tomography (CT) done on a GE 9800 scanner (General Electric, Milwaukee, Wis) showed multiple enlarged lymph nodes, most of which had a peripheral rim of calcification (Fig 1). These calcifications were not present on CT studies done before the interferon therapy. He was restarted on this medication and has shown a modest response to therapy in the past 2 months.

Discussion

Sinus histiocytosis with massive lymphadenopathy was described in 1969 by Rosai and Dorfman and is often referred to as *Rosai-Dorfman disease* (27). The average age of the patient at the time of disease onset is 20 years. The cause is unknown; it is currently classified as an idiopathic histiocytosis, although most

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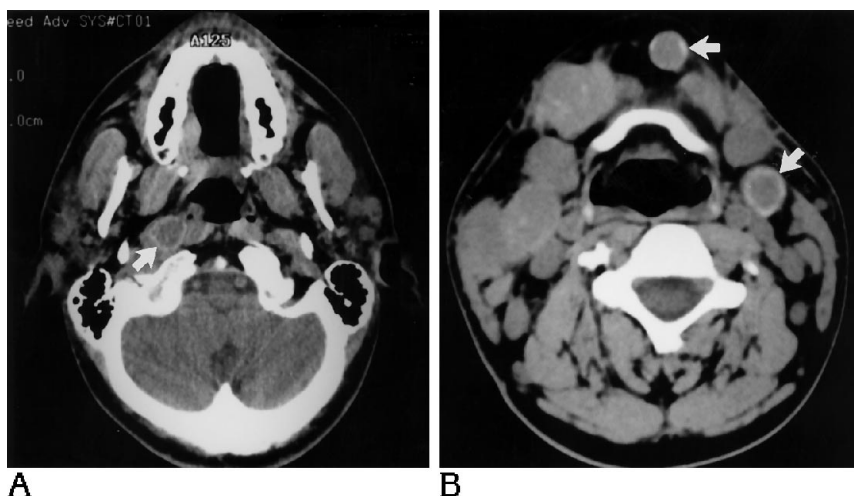
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Fig 1. A, Axial noncontrast CT scan at a level just beneath the skull base shows peripheral egg shell calcification (*arrow*) in an enlarged right retropharyngeal lymph node.

B, Axial noncontrast CT scan at the level of the hyoid bone shows peripheral egg shell calcifications (*arrows*) in submental and internal jugular chain lymph nodes.



recent reports appear to indicate that it is an autoimmune process. More than 85% of patients present with cervical lymphadenopathy, typically bilateral, nontender, and painless. Although in sinus histiocytosis with massive lymphadenopathy adenopathy is most common in the neck, enlarged nodes also can be found in the axillary, inguinal, and mediastinal nodal groups (27). Extranodal disease is seen in approximately 30% of patients, with the head and neck region comprising most such sites (28–30).

The most common CT finding in patients with sinus histiocytosis with massive lymphadenopathy is massive bilateral cervical lymphadenopathy involving any of the major nodal chains, with some nodes measuring up to 6 cm. The nodes usually are homogenous and enhancing, with no other distinguishing characteristics either on CT, magnetic resonance, or sonography (28–31). The differential diagnosis usually includes lymphoma and an infectious process.

Sinus histiocytosis with massive lymphadenopathy is typically self-limited, with approximately 20% of patients showing complete spontaneous remission. However, patients may require treatment including surgery, radiation therapy, or chemotherapy because of severe disease manifestations (32). However, no large studies of treatment regimens for sinus histiocytosis with massive lymphadenopathy have been performed, and most treatments are based on protocols for hematopoietic malignancy or Langerhans cell histiocytosis.

In the case presented, the patient's initial CT before treatment showed bilateral homogenous enhancing cervical lymphadenopathy. After

treatment with interferon, most of the lymph nodes demonstrated peripheral calcification in a pattern typical for egg shell calcification. This appearance has not been described in either sinus histiocytosis with massive lymphadenopathy or in patients treated with interferon. Egg shell calcification of lymph nodes is most commonly seen in the hilar and mediastinal nodes of patients with silicosis; however, similar mediastinal lymph nodes have been reported in sarcoidosis, scleroderma, and tuberculosis (14–16, 20–22). However, none of these diseases has been described as producing egg shell calcifications in the cervical nodal groups. Calcification of cervical lymph nodes can be seen in patients with tuberculosis, metastatic thyroid carcinoma, treated lymphoma, and a few other diseases. However the affected nodes typically do not demonstrate egg shell-type calcifications. Egg shell-type calcification has been described in the neck as a sign of parathyroid adenoma and thyroid carcinoma, but this is nonnodal calcification (23, 24).

The patient was not significantly immunosuppressed, so it is unlikely that these cervical nodal calcifications represent an underlying opportunistic infection. This patient demonstrated such egg shell calcifications only after therapy with interferon, and it appears that this calcification is related to the interferon treatment. However, it is unclear why interferon might cause egg shell calcifications. In patients with Hodgkin disease in whom nodal calcifications develop after chemotherapy or radiation therapy, the calcifications are felt to be dystrophic in nature, secondary to cellular necrosis (10–12). However, this scenario seems unlikely in

the present case, because CT did not suggest any central nodal necrosis. However, there may have been cellular necrosis on a more microscopic level. Histologic study of the egg shell calcified nodes is not available, because the patient responded clinically to a second course of interferon and there was no clinical reason to obtain a new nodal biopsy. It would be interesting to evaluate prospectively whether this type of nodal calcification is the result of the combination of sinus histiocytosis with massive lymphadenopathy and interferon or if it is a more generalized process that may be seen in any patient treated with interferon.

In conclusion, we report the finding of egg shell calcification in cervical lymph nodes in a patient with sinus histiocytosis with massive lymphadenopathy following treatment with interferon. Pretreatment CT showed no evidence of such calcification. Thus, the radiologist should be aware of this cause of egg shell nodal calcification and include it in the differential diagnosis of this finding.

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