Skeletal Imaging of Gorlin's Syndrome

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Key Words

Gorlin's syndrome · Basal cell nevus syndrome · Gorlin-Goltz syndrome · Nevoid basal cell carcinoma syndrome · Scintigraphy

Abstract

Objective: To report a case of a patient with many of the common manifestations of Gorlin's syndrome, a rare inherited condition. **Clinical Presentation and Intervention:** A 26-year-old female with longstanding left hip pain was referred for bone scintigraphy to find the cause of pain. The findings on bone scintigraphy as well as prior radiographic studies illustrated many of the defining features of Gorlin's syndrome, i.e. jaw keratocysts, falcine calcifications, short and deformed ribs, Sprengel deformity and a sclerotic bone lesion. The past medical history also revealed dermatologic, cardiac and gynecological findings related to the syndrome. **Conclusion:** Our case highlights the multisystemic involvement of Gorlin's syndrome, based particularly on the skeletal findings. Practicing physicians, including imaging specialists, should be familiar with these findings to reach the diagnosis.

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Introduction

Gorlin's syndrome is a rare familial condition. It is known by several other names, including basal cell nevus syndrome, nevoid basal cell carcinoma (BCC) syndrome

and Gorlin-Goltz syndrome. Gorlin's syndrome is a multisystemic entity and the diagnosis is usually established by the presence of major and minor criteria. The major criteria include a positive family history, presence of BCCs, jaw keratocysts, palmar or plantar pits and falcine calcifications [1–4].

Case Report

A 26-year-old African-American woman was referred to the Department of Nuclear Medicine for evaluation of long-standing left hip pain. Prior to scintigraphy, the patient had radiographs and a computed tomography examination of the hips. These studies demonstrated a sclerotic lesion in the left femoral neck (fig. 1a, b).

The patient was injected with 25 mCi (925 MBq) of technetium-99m hydroxyl diphosphate. Subsequent whole body imaging, as well as planar images of the ribs, skull, pelvis and hips were obtained 3 h after injection. Focal moderately intense increased uptake was seen in the proximal portion of the left femoral neck (fig. 2a, b), corresponding to radiographic and CT findings (fig. 1a, b). Intensely increased uptake was also observed in the bilateral maxillae, an abnormal high riding left scapula, and multiple deformed ribs (fig. 2c).

Reinterviewing the patient uncovered a history of removal of cysts from the sinuses 3 months prior to imaging. This included enucleation of bilateral maxillary cysts, with bone reconstruction, removal of a left mandibular cyst and repair of impacted molars. The cysts proved to be keratocysts by histology, and the diagnosis of Gorlin's syndrome was made at this time. Investigation into the patient's past medical history revealed additional findings consistent with Gorlin's syndrome. She had been followed for an elevated scapula (Sprengel's deformity) since childhood. At the age of 16, she had bilateral oophorectomy for ovarian fibromas. On physical examination, she had an elevated left scapula, palmar pits and a heart murmur secondary to previously diagnosed aortic stenosis.

Fig. 1. a Hip radiograph demonstrates a well-defined sclerotic lesion in the left femoral neck (arrowhead). **b** Pelvic noncontrast axial CT localizes the lesion to the posterolateral portion of the femoral neck (arrowhead). A second, smaller sclerotic lesion is present in the contralateral femur (arrow).

Fig. 2. a Anterior whole body technetium-99m hydroxyl diphosphorates image demonstrates intense maxillary uptake, status after enucleation of bilateral maxillary keratocysts, left Sprengel's deformity and bilateral rib abnormalities. **b** Spot planar image of the pelvis shows femoral neck lesion with moderately increased activity (arrow), corresponding to abnormality on radiograph and CT scan (fig. 1). **c** Left anterior oblique image showing shortening of the first five left ribs (arrowheads). Note the bifid left 9th rib (arrow).

Fig. 3. **a** Preoperative axial CT of the facial bones demonstrates bilateral fluid-containing expansile maxillary cysts (arrows). **b** Axial CT of the skull shows a ring of calcification (arrows) in the tentorium.

She denied history of BCC or any family history of Gorlin's syndrome. Review of prior imaging revealed jaw keratocysts, calcification of the falx and tentorium, Sprengel's deformity and spina bifida occulta (fig. 3a, b).

After speaking with the patient and reviewing her history, the findings on bone scintigraphy, including the region of focally increased uptake in the left femoral neck, were believed to be part of Gorlin's syndrome.

Discussion

Gorlin and Goltz [5] described this rare syndrome in 1960, with an earlier case report by Jarisch and White in 1894 [6]. It is an autosomal dominant condition, with complete penetrance and variable expressivity that has been mapped to chromosome 9. Multiple organ systems are affected and diagnosis is usually confirmed within the first three decades of life.

Diagnosis requires the presence of some combination of major and minor criteria. The most frequently cited major criteria include positive family history, BCCs, jaw keratocysts, palmar or plantar pits (indentation, pock mark or depressed scar) and falcine calcification [1, 5, 7]. Various studies describe a variety of minor criteria, involving the central nervous, cardiovascular, genitourinary and musculoskeletal systems.

Up to 75% of patients are affected by odontogenic keratocysts. These are more common in the mandible than in the maxilla [1]. Histologically, these epithelial lined cysts contain columnar or cuboid cells which are keratinized. Keratocysts are more aggressive than other jaw cysts. After removal, recurrence is common. In Gor-

lin's syndrome, the cysts may appear in the first decade of life, but peak occurrence is in the second to third decade.

BCCs are the most characteristic and worrisome findings in Gorlin's syndrome. BCCs are known for occurring in large numbers and at a young age. As BCCs are seen in 80–90% of Caucasians, but only about 40% of African-Americans, it is postulated that skin pigmentation may have a protective role in the development of BCCs [1, 8]. The other common skin manifestation is palmar and plantar pits, which are caused by defects in the stratum corneum.

CNS abnormalities are present in 85% of patients. Calcifications in the falx cerebri and, to a lesser extent, the tentorium cerebelli are the most common of these findings. Medulloblastoma is the most commonly associated CNS tumor, usually presenting in the first 3 years of life [1]. Meningiomas are also seen, but less frequently.

There are numerous skeletal abnormalities. Sixty percent of these patients have splayed cervical or bifid ribs [1]. The third to fifth ribs are most often involved. Spina bifida occulta has been reported in up to 60% of patients in some series [2, 9]. When present, the spina bifida most frequently involves the cervical or thoracic spine. Up to 11% of patients with Gorlin's syndrome have a Sprengel's deformity (elevation of the scapula due to failure to descend to its normal position during fetal life) [1]. Other reported associations include scoliosis, cervical ribs, pectus deformity, short 4th and 5th metacarpals, polydactyly and craniofacial anomalies such as frontal bossing, macrocephaly and hypertelorism.

Lytic and sclerotic bone lesions have also been described [10]. Flame-shaped lucencies may be seen in the hands and feet [1, 3]. Sclerotic bone lesions that resemble bone islands or enostosis can also be seen, but their pathogenesis is unknown [11]. The lesion seen on our patient's bone scan and CT of the left hip is an example of such lesions. The most clinically important differential is metastatic BCC. However, this is very rare, and such metastatic lesions are more often lytic. Bone scintigraphy may be helpful in differentiating these entities [11].

Since Gorlin's syndrome does involve multiple organ systems, affected patients may be referred for imaging by a diverse group of clinicians, including pediatricians, orthopedic surgeons, gynecologists and dermatologists. Im-

aging specialists such as radiologists and nuclear medicine physicians should be familiar with the criteria of Gorlin's syndrome to aid clinicians in the diagnosis and avoid possible confusion with other scintigraphic diagnosis, including metastatic disease.

Conclusion

This patient demonstrated many of the manifestations of Gorlin's syndrome, including keratocysts, falcine calcification, palmar pits, Sprengel's deformity, bifid ribs, spina bifida, aortic stenosis, ovarian fibromas and sclerotic bone lesions.

References

- 1 Kimonis VE, Goldstein AM, Pastakia B, et al: Clinical manifestations in 105 persons with nevoid basal cell carcinoma syndrome. *Am J Med Genet* 1997;69:299-308.
- 2 Gorlin RJ: Naevoid basal-cell carcinoma syndrome. *Medicine* 1987;66:96-113.
- 3 Dunnick NR, Head G, Peck GL, Yoder FW: Nevoid basal cell carcinoma syndrome: Radiographic manifestation including cyst-like lesions in of the phalanges. *Radiology* 1978;127:331-334.
- 4 Shanley S, Ratcliffe J, Hocky A, et al: Nevoid basal cell carcinoma syndrome: Review of 118 affected individuals. *Am J Med Genet* 1994;50:282-290.
- 5 Gorlin RJ, Goltz RW: Multiple naevoid basal-cell epithelioma, jaw cysts and bifid rib. *New Engl J Med* 1960;262:908-912.
- 6 Hall J, Jonston KA, McPhillips JP, Barnes SD, Elston DM: Nevoid basal cell carcinoma syndrome in a black child. *J Am Acad Dermatol* 1998;38:363-365.
- 7 Evans DGR, Ladusaris EJ, Rimmer S, Burnell LD, Thakker N, Farndon PA: Complications of the naevoid basal cell carcinoma syndrome: results of a population based study. *J Med Genet* 1993;30:460-464.
- 8 Korczak JF, Brahim JS, DiGiovanni JJ, Kase RG, Wexler LH, Godstein AM: Nevoid basal cell carcinoma syndrome with medulloblastoma in an African-American boy: a rare case illustrating gene-environment interaction. *Am J Med Genet* 1997;69:309-314.
- 9 Ratcliffe JF, Shanley S, Chenevix-Trench G: The prevalence of cervical and thoracic congenital skeletal abnormalities in basal cell naevus syndrome; a review of cervical and chest radiographs in 80 patients. *Br J Radiol* 1995;68:596-599.
- 10 Blinder G, Barki Y, Pezt M, Bar-Ziv J: Widespread osteolytic lesions of the long bones in basal cell nevus syndrome. *Skeletal Radiol* 1984;12:196-198.
- 11 Yee KC, Tan CY, Bhatt KB, Davies AM: Case report: sclerotic bone lesions in Gorlin's syndrome. *Br J Radiol* 1993;66:77-80.