DX: Midline Carcinoma with BRD4-NUT rearrangement - 5% of respondents

Other Diagnosis: Malignant Rhabdoid Tumor 85%; Epithelioid Sarcoma 5%; Ewing’s Sarcoma 5%; Neuroblastoma 2%

Q1: (C) 7% (B) 85% (D) 6% (A) 2%
Q2: (D) 5%* (B) 90% (C) 4% (A) 1%
Q3: (C) 6% (D) 86% (B) 7% (A) 1%

* Note: Error (HM) in option D to include thyroid as a possible primary site, thus far not reported in the literature.

The sections show a high-grade malignancy with primitive - undifferentiated morphology, infiltrating dermis and subcutaneous soft tissues. This tumor has no particular pattern of growth or specific apparent line of differentiation. Cytologically it corresponds to primitive cells, some with cytoplasm including rhabdoid features. Focal areas show myxoid background and short spindle-cell morphology. No matrix assembled, no evidence of squamoid or epithelial, glandular or organoid differentiation. A vague alveolar pattern is focially discerned. Immunohistochemistry showed variable, focal but strong positivity for vimentin, CK 18, CD99, AE1/AE3 and CD34, and evident nuclear expression of INI1 (BAF47) throughout. Markers for Epithelial Membrane Antigen, actin, desmin, myogenin and CD45 were negative. Cytogenetics revealed various abnormalities including a distinctive chromosomal translocation t(15;19)(q15;p13.1) resulting in the fusion of BRD4-NUT oncogene confirmed by FISH (at Dr. French’s Laboratory, Boston MA), establishing this diagnosis.

Because of the lack of epithelial differentiation, the differential diagnosis genuinely includes many of the poorly differentiated neoplasms including neuroendocrine and myoepithelial carcinomas and many sarcoma variants, including all diagnosis submitted by the contributors. The value of this case is to increase the awareness of this very rare but increasingly recognized tumor in different sites, as a potentially misleading alternative. Except for diffuse expression of INI1, the focal positivity of the other markers makes this tumor difficult to diagnose, particularly in limited biopsy specimens. In fact, NUT Midline Carcinomas should be entertained and NUT-gene rearrangement explored in “any poorly differentiated, monomorphic midline neoplasm that does not stain for lineage-specific markers” French, C.A. 2008.

Midline Carcinoma with NUT rearrangement is a rare, highly malignant neoplasm which has been now reported in multiple sites including the urinary bladder, and usually within the midline. It is defined exclusively by this cytogenetic translocation t (15; 19)(q14; p13) and NUT gene rearrangement as its molecular genetic signature. Involvement of the lung thus far appears to represent extension from mediastinal primaries according to the most recent review by French. NUT variant carcinoma represents tumors with other than BRD4, which tend to show more evident squamoid differentiation and possibly a less aggressive course.

An example of undifferentiated thymic carcinoma with t(15;19)(q15;p13) was originally described by Kubonishi et al. The tumor presented as superior vena cava syndrome in a 22-year-old female and pursued a rapidly progressive course with widespread metastases. Despite combined chemotherapy and radiation, the patient died 4 months after diagnosis. Only focal EMA and cytokeratin was expressed by an otherwise undifferentiated tumor composed of small cells with prominent nuclei; the tumor showed focal squamoid differentiation. When present, this feature seems to be the only clue that an undifferentiated carcinoma is in the working differential diagnosis.

The gene fusion resulting from this distinctive translocation, was characterized by French et al., in 2001. The breakpoint interrupting the bromodomain gene BRD4 or BRD3 located in chromosome 19 p13.1 was identified in a study of two cell lines from tumors arising in the mediastinum and the epiglottis. These two and four other tumors identified tumors presented in patients ranging from 5 to 34 years of age, pursued a rapidly aggressive clinical course. The morphology was consistently similar and included on case with glandular differentiation. Originally termed MCAP (Mitotic Chromosome-Associated Protein), the function of BRD4 appears to mark actively transcribed genes before mitosis. The partner NUT (nuclear protein in testis) was later identified in 2004, where the authors identify 11 cases out of 98 examples of poorly differentiated carcinomas in young patients. Eight of these with only the NUT gene rearranged (NUT variant), and propose the currently accepted designation for these tumors as Midline Carcinoma with NUT rearrangement or NUT rearranged carcinomas. The relatively consistent expression of CD34 suggests that these tumors may arise from epithelial progenitor-cell rests according to the authors.

There are two reports of successful therapy. A 10 year old with an iliac bone-primary tumor with BRD4-NUT fusion treated with a Ewing's sarcoma protocol including radiation, currently in remission. The other reported patient is a 30-year-old woman with a poorly differentiated mediastinal tumor with glycogen-
containing cells. This tumor was unresponsive to initial Ewing's sarcoma therapy, requiring radiation and docetaxel which resulted in a dramatic tumor response.

The unusual 15-year survival of the patient with the iliac bone NMC is according to most recent review by French, C.A., is due to "unusual characteristics of the tumor, and not due to fortuitous treatment with a regimen that is generally effective in NMC". A recent series of 31 undifferentiated carcinomas occurring in the upper aerodigestive tract identified 5 cases unassociated with EBV, having the BRD4-NUT rearrangement, many of which previously diagnosed as sinonasal undifferentiated carcinoma. The age range of these tumors was 31-78 years, average age 47 years. This article highlights the wide age-range for NMC.

Whether this entity is a carcinoma or a malignancy with a primitive morphology and polyphenotypic immunohistochemical profile with epithelial differentiation remains to be elucidated. The definitive diagnosis however, rests on the identification of the gene fusion by FISH, RT-PCR or the documentation of the translocation by conventional cytogenetics, and should be sought in unclassifiable primitive malignancies, in children, adolescents and adults.

References:

French, C.A., Demystified Molecular Pathology of NUT Midline Carcinomas. JCP Online First, Published June 13 2008 as 10.1136/jcp.2007.052902


Infantile myofibromatosis (IM) is the most common benign fibroblastic-myofibroblastic proliferation in infancy, with approximately 90% of cases occurring within the first 2 years of life, including some which are present at birth. IM shares with many other soft tissue tumors the distinction of multiple different names or "appellations"; but the designation of "infantile myofibromatosis" by Chung and Enzinger in 1981 has remained a fixture in the pediatric pathology literature. The majority of cases (~65-80%) are solitary nodules or masses (i.e., myofibroma or solitary myofibroma) and occur most frequently in males, while the remainder (20-35%) are multicentric proliferations (myofibromatosis) and predominate in females (although this is not a uniform finding in all series). The multicentric lesions tend to be more clinically aggressive, with a higher predilection for visceral involvement. The tumor occurs most commonly within the skin (dermis) or subcutaneous tissues of the head and neck regions but is also seen in the trunk and proximal parts of the upper and lower extremities; it may also arise from the deep fascia, skeletal muscle, or even bone. The prognosis of solitary infantile myofibroma (as opposed to the multicentric visceral form) is excellent, with frequent instances of spontaneous regression and a recurrence rate ranging from ~7-13%; re-excision of recurrence is usually curative. The outlook for the multicentric visceral form is notoriously unfavorable, with considerable morbidity and a mortality rate ranging from 20% cited in Chung and Enzinger's original series to 76% in a subsequent 1985 series).

Grossly, the tumor is typically a sharply circumscribed but unencapsulated nodule or mass with a lobulated, firm, sometimes gritty cut surface and occasional hemorrhagic foci. Microscopically, it displays a characteristic biphasic pattern, consisting of a central hemangiopericytomatous component with numerous proliferating blood vessels (often in an irregularly branching, "staghorn" configuration) and densely cellular aggregates of intervascular pericyte-like cells.; and a peripheral element comprised of short fascicles of bland spindle cells (myofibroblasts), whose cellularity is almost always less than that present within the central portion of the lesion,. However, in some instances, the various proportions of the central and peripheral components are unequal, and either component may be entirely absent, making the lesion more difficult to recognize and diagnose. When the central component undergoes regressive change, the lesion appears as a myofibroblastic lesion with necrosis, dystrophic calcification, or other degenerative feature(s) (i.e., cystic change). When the hemangiopericytomatous component predominates or is unaccompanied by the peripheral myofibroblastic element, the designation of "infantile hemangioendothelioma" has been used in the past. Additionally some tumors, including the one presented in this slide survey, exhibit a distinctive pattern of concentric perivascular growth of "myoid" cells, with morphologic and immunophenotypic features between myofibroblasts and smooth muscle cells, thus accounting for the "myopericytoma" designation. Mitotic activity may be present (up to ~8 per 10 high-power fields) but atypical mitotic figures are not seen.

The immunophenotypic profile is somewhat variable; while virtually all of the cells, including the central round inter- and perivascular cells and peripheral spindled myofibroblastic cells uniformly expressing alpha-smooth muscle actin but desmin expression in some but not all cases. One school of thought proposes that...
desmin expression represents a marker of maturation of myofibroblasts along a path of smooth muscle differentiation.

Although an interstitial deletion of 6(q12q15) has been described in IM in the literature, no consistent patterns of cytogenetic or molecular genetic abnormalities have been documented in cases of IM.

In 1994, Mentzel et al. described a series of 11 infants and children, ranging in age from 6 days to 7 years, but 7 of whom were less than one (1) year of age, all of whom were given an original pathologic diagnosis of infantile hemangiopericytoma. However, when the authors reviewed these tumors, they observed, in addition to the hemangiopericytomatosus features, also a second element consisting of bundles and nodular arrangements of spindled cells with features of myofibroblasts. Furthermore, although morphologically distinct, both the spindled cells and the round pericytes exhibited immunopositivity with antibodies to alpha-smooth muscle actin, suggesting some commonality of differentiation. The authors concluded that infantile myofibroma(tosis) and infantile hemangiopericytoma were actually variations along a spectrum or continuum of the same pathologic entity (disease process); specifically, the more primitive-appearing round cells with the hemangiopericytoma-like vascular pattern represented an earlier (younger) stage of differentiation or maturation than the spindled myofibroblastic component.

To complicate matters, the term “myopericytoma” was introduced in the literature in 1998 by Granter et al. to denote lesions with characteristics of both hemangiopericytoma and glomus tumors; but once again, the concept of an ontogenetic spectrum was espoused among the entities of IM, glomangiopericytoma, and myopericytoma, with the common feature being that of perivascular myoid differentiation. Finally, in 2006, Mentzel et al. readdressed this issue and concluded that myopericytoma was indeed a unique pathologic entity namely, a “distinct perivascular myoid neoplasm…characterized by the presence of numerous thin-walled blood vessels concentrically surrounded by ovoid, plump spindled, and/or round myoid tumor cells showing a broad morphologic spectrum”. Curiously, h-caldesmon expression was documented in the perivascular myoid cells (observed only rarely and focally in cases of IM).

The tumor in the case presented above contains elements of both hemangiopericytoma-like and myopericytoma-like patterns, as defined above, the former with irregularly branching “staghorn-like” vessels and the latter with concentric perivascular growth around small rounded vessels resembling an onion-skin arrangement. Yet, as was emphasized in Mentzel et al's 2006 study, the immunophenotypic profile of the intervascular cells within both areas was virtually the same – suggesting once again a commonality of differentiation. Ultimately, which particular name one chooses to assign a lesion like this rests largely on the nature of the pathologist; a “splitter” may choose to get fancy, referring to this as a hybrid tumor with hemangiopericytoma-like and myopericytoma-like features; while a lumpers may simply choose to designate this lesion as a “benign myofibroblastic lesion – see comment”.

REFERENCES


The glycogen storage diseases (GSD) form a large heterogenous group of metabolic disorders resulting in impaired glycogen degradation or production, resulting in abnormal glycogen accumulation, primarily in the liver, skeletal muscle, cardiac muscle, and nervous system. The forms involving the liver include types I, III, IV, VI, and IX. Glycogen storage disease type IV, also called Andersen's disease or amylopectinosis, is a rare autosomal recessive form caused by a deficiency of the glycogen branching enzyme (alpha-1,4-glucan:alpha-1,4-glucan 6-glycosyl transferase) encoded by the GBE1 gene on chromosome 3p14. The abnormal glycogen produced is an amylopectin-like polysaccharide with reduced branching points and increased chain length. Liver involvement in GSD type IV is characterized by intracytoplasmic inclusions resembling Lafora bodies, a feature which helps to distinguish type IV from other types of GSD. These inclusion bodies tend to be most prominent in periporal areas. In contrast, GSD types I and III characteristically show clear glycogenated hepatocellular cytoplasm and a "mosaic tile" pattern formed by distended hepatocytes compressing intervening sinusoids. Glycogenated nuclei are common in GSD types Ia and III, but are not typically seen in GSD type IV. Periodic acid Schiff stain is used to demonstrate glycogen accumulation in hepatocytes in all forms of GSD affecting the liver, and the inclusions of GSD type IV are PAS-positive and diastase-resistant. The inclusions may be digested with alpha-amylase. Colloidal iron is an additional stain which is most useful in demonstrating the amylopectin in the cytoplasmic inclusions of GSD type IV. Electron microscopy demonstrates abundant fibrillar glycogen material, admixed with polyparticulate alpha rosette glycogen.

Various clinical forms include a congenital neuromuscular form, childhood neuromuscular form, adult neuromuscular form with isolated myopathy, and rarely a non-progressive hepatic form with survival into adulthood. In its classic form, progressive hepatomegaly and hepatic fibrosis occur in the first 18 months of life, with death by age 5 years. Hypoglycemia, acidosis, failure to thrive, muscle weakness, and myopathy are common, and some children also develop a cardiomyopathy. Although liver biopsy is helpful in characterizing GSD type IV, definitive diagnosis depends on assay for branching enzyme activity in a skin fibroblast culture (0 nmol/min/mg protein; normal 1300 +/- 390 nmol/min/mg protein). The explanted liver weighed 523 grams (418 grams expected for age) and had a smooth capsular surface. The cut surface was homogenous and light brown without gross nodularity or other focal lesions. The gallbladder contained approximately 20 cc of golden yellow bile. Microscopically, scattered hepatocytes contained globular pale eosinophilic cytoplasmic ground glass inclusions. Numerous clusters of hepatocytes were distended by clear cytoplasm and produces collapse of intervening sinusoids and a "mosaic tile" pattern. PAS stain was negative in areas of hepatocellular clearing, but highlighted PAS-positive globules. Colloidal iron was positive (insert) in the hepatocyte inclusions. There was no evidence of hepatocellular necrosis. The hepatic architecture was altered by diffuse mild portal and lobular fibrosis, with focal bridging fibrosis and a suggestion of micronodularity. Patchy mild lymphocytic inflammation and small lightly-pigmented macrophages were associated with portal tracts. Electron microscopy of the hepatocytes showed abundant fibrillar material with small amounts of interspersed particulate glycogen. Small amounts of lipid and minimal cytoplasmic degeneration were also noted.

The differential diagnosis of GSD type IV in the liver includes Lafora disease, hereditary fibrinogenemia, cyanamide alcohol aversion therapy, and Lafora-like bodies in transplant patients. Lafora disease is distinguished clinically, typically presenting in late childhood or adolescence with a triad of epilepsy, myoclonus, and dementia. Like the hepatocyte inclusions of GSD type IV, Lafora bodies are colloidal iron-positive, but are less coarsely clumped than in GSD type IV. Hereditary hypofibrinogenemia (fibrinogen storage disease) produces similar eosinophilic hepatocellular cytoplasmic inclusions due to endoplasmic reticulum storage of fibrinogen. Cyanamide therapy is associated with similar hepatocellular inclusions, but is easily excluded by patient age and clinical history. In recent years, it has been recognized that Lafora-like bodies may also occur in livers of patients after bone marrow transplant or solid organ transplant.
These inclusions are formed by non-membrane bound accumulation of hepatocellular glycogen. This phenomenon remains of unknown etiology, but has been suggested to result from abnormal glycogen metabolism related to polypharmacy.

References:

Grossly, the resected mass was markedly hemorrhagic but solid with a vague whorled appearance on the cut surface, and central superficial necrosis related to the prior biopsy site. Microscopically, the tumor is composed of cellular sheets and fascicles of compact slit-like vascular channels containing erythrocytes and erythrocyte fragments, resembling Kaposi sarcoma. The endothelial cells are plump with bland cytology. Frequent foci of extramedullary hematopoeisis and occasional hemosiderin deposits are distributed throughout this lesion. Platelet microthrombi are visible on H&E stained sections, and may be highlighted by CD61 staining. Mitotic activity is low. Dilated branching thin-walled vessels and lymphatic structures are interposed between regions of spindled cells, most prominently at the periphery and in the overlying reticular dermis. Occasional fibrous septa separate the large zones of vascular proliferation. The lesion appears encapsulated by fibrous tissue in some areas, and infiltrates into the surrounding connective tissue in other areas. Immunohistochemistry demonstrates expression of CD31 and CD34, as well as extensive expression of the lymphatic markers LYVE-1, VEGFR-3, and D2-40. Immunohistochemistry for the erythrocyte glucose transporter (Glut1) and HHV-8 are both negative, excluding infantile hemangioma and Kaposi sarcoma, respectively.

KHE has features of both a neoplasm and a vascular malformation, and its proper biologic classification remains unclear. Unlike infantile hemangioma, KHE does not show regression or involution, and the natural history is typically that of slowly progressive growth. KHE generally has been considered a neoplasm of indeterminate or borderline malignant potential based on rare reports of regional lymph node “metastases”, however some suggest that this lymph node involvement may represent multifocality in a lymphatic distribution, rather than evidence of malignant behavior. Indeed, KHE recently has been recognized to express the lymphatic marker D2-40, and is also described in association with lymphangiomatosis at other sites. Distant hematogenous metastasis has not been reported. Primary treatment for KHE is complete surgical excision, although larger unresectable lesions may be treated medically with a combination of steroids, interferon-alpha-2a, and/or vincristine. Mortality associated with KHE is low, but may result from complications of thrombocytopenia or direct tumor infiltration.

The differential diagnosis of KHE includes infantile hemangioma, congenital hemangiomas, vascular malformations, tufted angioma, Kaposi sarcoma, and other highly vascular spindled soft tissue sarcomas such as congenital-infantile fibrosarcoma and rhabdomyosarcoma. Infantile hemangioma is the most common vascular tumor in children, occurring in approximately 4-10% of infants. Infantile hemangioma is easily distinguished from KHE due to its lobular pattern and proliferation of small round capillaries rather than spindled cells. Clinically, infantile hemangiomas characteristically appear within a few weeks of life, but do not manifest as a mass lesion at birth, as in this case. Unlike KHE, the natural history of infantile hemangioma is characterized by a period of rapid proliferation over the first weeks of life, followed by slow regression and near-complete involution in the first year of life. Endothelial expression of Glut-1 is a diagnostic characteristic of infantile hemangioma, and is not a feature of KHE. The differential diagnosis of congenital KHE includes the congenital hemangiomas, including rapidly involving congenital hemangioma (RICH) and non-involving congenital hemangioma (NICH). RICH and NICH typically produce large cutaneous and subcutaneous violaceous plaques or masses which are fully developed at birth. Some may show central scarring, telangiectasia, or a peripheral halo. RICH lesions undergo rapid regression after birth, while NICH lesions typically fail to involute or undergo a period of limited regression. Like KHE, RICH and NICH are Glut-1 negative vascular lesions; however, unlike KHE, the congenital hemangiomas do not
express the lymphatic marker D2-40. The differential diagnosis of KHE includes vascular malformations, particular isolated or mixed venous malformations, which may be associated with thrombocytopenia. KHE is easily distinguished from these based on its high cellularity and the spindled nature of the cell proliferation. Tufted angioma is a superficial skin lesion with “cannonball” tufts of small vessels distributed in the dermis and subcutaneous tissue, associated with peripheral dilated lymphatic channels. This lesion may be difficult to distinguish from the superficial cutaneous form of KHE, and indeed it is theorized that tufted angioma has similar histogenesis to KHE and represents the most superficial form of this histologic spectrum. The spindled cells and compact vascular spaces of KHE may prompt consideration of Kaposi sarcoma morphologically, however Kaposi sarcoma is unlikely to produce a congenital mass, more typically occurring in older HIV patients or other immunocompromised patients. Kaposi sarcoma is also associated with HHV8 infection and plasma cell inflammatory infiltrates, features which are not seen in KHE. The clinical and diagnostic imaging differential diagnosis of KHE includes congenital-infantile fibrosarcoma and rhabdomyosarcoma, both of which may produce a large highly vascular soft tissue mass. These tumors are easily distinguished from KHE pathologically by their primitive hyperchromatic spindled cell morphology (“small spindled blue cell tumors”) and lack of formation of compact vascular channels. Immunohistochemistry for myogenin and/or myoD1 are confirmatory in rhabdomyosarcoma. Cytogenetic analysis demonstrating a t(12;15) translocation or molecular studies showing the characteristic ETV6-NTRK fusion product are also helpful in confirming a diagnosis of congenital-infantile fibrosarcoma.

References:

**DX: Gaucher’s Disease - Hemoglobin S-C Disease - 80% of respondents**

Other Diagnosis: Pseudo-Gaucher’s w/ infarcts 10%; Histiocytic Disorder / sequestration crisis 10%

Q1: (B) 80%  (A) 17%  (C) 3%
Q2: (A) 52%  (B) 43%  (C) 3%  (D) 2%
Q3: (D) 93%  (A) 6%  (C) 1%

Sections show extensive alterations in the spleen related to expansion of the splenic cords by a proliferation of histiocytes containing abundant, fine granular or slightly vacuolated cytoplasm with eosinophilic material. Tissue imprints stained with WG show grayish-blue granular cytoplasm. Congestion and evident sickling of erythrocytes distend the sinus spaces.

By ultrastructure the histiocytes contained elongated lysosomes and branching tubular inclusions, which average 50nm. After splenectomy, the patient underwent mutation analysis, demonstrating one copy of the 1448C (L444P) mutation. WBC glucocerebrosidase activity was low at 5.684 nanomoles/hr/mg protein (range 7.5-14.5 nanomoles/hr/mg protein) as evidence confirmatory of Gaucher’s Disease.

Gaucher’s Disease (GD) is a common lipid storage disorder that is inherited as an autosomal recessive manner. It is characterized by a significant reduction of glucocerebrosidase activity in cells, resulting in accumulation of glucosylceramide and other glycolipids within the lysosomes of the reticuloendothelial system. The gene encoding acid β-glucosidase (GBA) is located on the long arm of chromosome 1(1q21).

Many mutations of the gene have been identified, four mutations account for 80% cases, making targeted molecular genetic testing for these 4 mutations and seven other less frequent mutations highly reliable.

While the correlation of the clinicopathologic manifestations with the genotype of GD are not precise, an excellent review by Pastores and Hughes suggests several observations which help sub-classify and understand some of the variations of this disease, described as showing “… a continuum of clinical findings from a perinatal-lethal form to an asymptomatic form”.

Many of the pathologic manifestations depend on the type of GD. The accumulation of glucocerebroside occurs within the histiocytes of the reticuloendothelial system of the spleen, lymph nodes, bone marrow, lung, brain and liver. In the placenta, storage material can be identified within intravillous region cells or in Hofbauer cells.

There main or relatively distinct clinical forms of GD include:

**Type 1 (non-neuronopathic):** presents usually in later childhood and adolescence, may present shortly after birth or in adulthood. Manifestations include painless splenomegaly, thrombocytopenia, anemia and leukopenia. Bone involvement includes acute or chronic bone / joint pain, flaring of the femoral metaphysis and epiphysis (flask deformity), osteopenia, lytic or sclerotic lesions and osteonecrosis, it can be a primary limiting manifestation in some patients. Cutaneous and renal involvement may be seen. Some patients may have secondary neurologic impairment related to vertebral collapse, emboli or coagulopathy. Lung involvement may be related to interstitial, intraalveolar and intravascular Gaucher-cell infiltration.

**Type 2:** (acute neuronopathic, infantile) – typically presents as a severe, rapidly progressive neurologic dysfunction usually within the first six months of life, but its spectrum overlaps with type 3 below.

**Type 3:** (subacute juvenile neuronopathic, Swedish or Norrbottian) – presents later in childhood, manifesting with ataxia, spasticity, akinetic and myoclonic seizures, and variable degrees of dementia.
**Perinatal-lethal:** associated with hepatosplenomegaly, pancytopenia, arthrogryposis and ichthyosiform skin changes.

**Cardiovascular:** consisting of calcification of the mitral and aortic valves, associated with oculomotor apraxia, bone disease, corneal opacity and mild splenomegaly.

The diagnosis of GD is established by documentation of decreased GBA activity in leukocytes or tissue cells, including chorionic villi, and molecular genetic sequencing probing for known mutations.

Therapy for GD includes enzyme replacement with exogenous glucocerebrosidase, splenectomy in patients with splenomegaly and / or thrombocytopenia, transfusion, analgesics and joint replacement. Bone marrow transplantation is usually limited to individuals with severe GD. Gene therapy may offer better results in the future, particularly in type 2 and 3 GD, since exogenous enzyme does not cross the blood-brain barrier.

Hemoglobin SC Disease occurs in the same frequency as that of Hb SS disease in African American individuals. The clinical manifestations are usually milder; splenomegaly may be the most conspicuous finding.

The coexistence of GD and Sickle Cell Trait as seen in this patient appear to be coincidental, but highlights the difficulty in clinical diagnosis when symptomatology is attributed to an underlying disease capable of showing similar manifestations. A literature search combining both diagnoses retrieves a few reviews highlighting the vertebral body collapse in GD and growth abnormalities in sickle cell beta-thalassemia as a common denominator in these two diseases.

References:


