Caffey's Disease: A Diagnostic Dilemma

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Caffey-Silverman disease is a rare self-limiting disease of early infancy which can cause diagnostic dilemma as well as considerable anxiety to the parents and the treating physician. Possible difficulties include traumatic disorders, bone infection, hypervitaminosis A, scurvy and primary and metastatic bone diseases.

We present the case of a one and a half months old male child who presented with a painful swelling of his right leg. Over a follow up period of one year, the possibility of several aforementioned differentials were entertained and ruled out. There was spontaneous and complete resolution of the mass and the final functional and radiological outcome at one year follow up were excellent.

Keywords: caffey disease, diagnostic dilemma, infantile cortical hyperosteosis.

Caffey-Silverman disease also known as Infantile Cortical Hyperosteosis and Caffey Syndrome is a self-limiting disease of early infancy that is characterized by a triad of soft tissue swelling, cortical thickening of the underlying bone and hyperirritability.[1]

Case Report

We report a case of a one and half months old male child who presented to our center with chief complains of painful swelling of the right leg for ten days. There was no history of trauma or fever but the child had been irritable for the last six days. The parents were understandably very anxious as the possibility of infection and malignancy had already been raised at other center. The antenatal, perinatal, postnatal and family history were consistent for a first born full term normal delivery child. His immunization was up to date.

Clinical examination revealed normal healthy an irritable, afebrile baby with a

uniform tender swelling of the entire of the right leg. The swelling was firm, immobile and the overlying skin was normal. Radiographic examination showed hypertrophic callus formation of the right fibula.

The child was admitted and investigated further. The laboratory tests showed an ESR of 18 mm/hr, C-reactive protein of 2.9 mg/L, WBC count of 9,100 with predominant lymphocytosis. His hemoglobin was 8.6 mg% and serum alkaline phosphatase was 1540 IU/L with normal serum calcium and phosphorus.

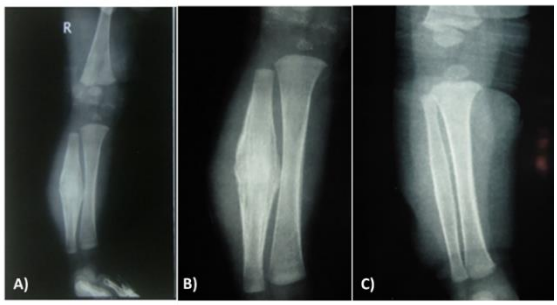

Figure 1: Serial X-ray pictures of the child showing progression of the disease, A) X-ray at the time of presentation showing diffuse thickening of fibula with periosteal reaction, B) X-ray of the same child after 3 months of onset of disease showing increase in the size of bones with periosteal reaction, C) X-ray after one year showing healing of the disease

USG of right leg showed an abscess in the right calf abutting the posterolateral surface of the fibula with thickening of the periosteum of the fibula.

One month later the child had enlarged swelling with mild fever. His ESR was 45mm/hr, WBC count of 10,400 with lymphocytic predominance, hemoglobin of 9.1 gm%. X-ray showed enlargement of fibula with periosteal reaction **(Figure 1).** MRI showed diffuse muscle enlargement with loss of normal signal intensity, enlarged fibula with periosteal reaction and a new bone formation **(Figure 2)**.

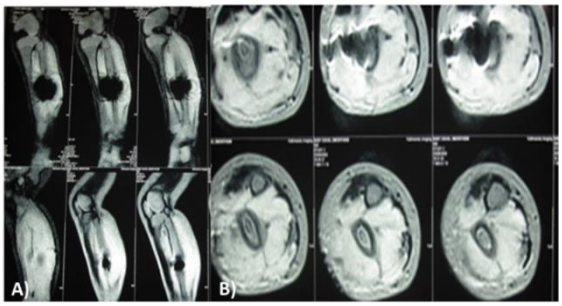

Figure 2: MRI of the right leg during active stage of disease, A) T1W MRI, coronal section showing enlargement of shaft of fibula with periosteal reaction and formation of new bone without marrow signal changes, B) Axial section showing the same changes

Biopsy showed thickened (reactive) bony trabeculae with intervening marrow and adjacent fibromuscular soft tissue with focal myxoid change and mild lymphocytic infiltration with no evidence of neoplasm.

Over the following weeks, the fibular (leg) swelling continued to increase in size. Three months later all the lab reports became normal. There was spontaneous and complete resolution of the lesion after five months and no recurrences at one year.

Discussion

Caffey disease was first described by Caffey and Silvermann in 1945.[1] A similar entity had already been reported by Roske and by Ellis in 1930 and 1938 respectively.[1] The incidence of the disease is 3/1000 infants under 6 years of age.[2] Caffey disease affects infants in the first 5 months of their lives, although it has also been described at birth and even in utero.[2]

The onset of disease is usually before 5 months of age and resolution is complete by 3 years of age.[3]

Etiology

The etiology remains unknown and different factors have been attributed in its causation including genetic aberration, infection and allergy.

According to the genetic basis it is of two types. Sporadic type is less common which predominantly involve the mandible (about 75% to 80% of cases).[3] Familial type is inherited as autosomal dominant, involving the younger infants.[3] There is a possible hereditary defect of arterioles of periosteum.[1]

The constitutional signs similar to bacterial and viral infection are associated with caffey disease[4] but none has been isolated[1] and the serological tests for infection are usually negative.[1]

An allergic basis has also been postulated as a cause of Caffey disease because of the response of the disease to corticosteroid and precipitation of the symptoms with dietary changes.[1] This lesion has also been described in infants who receive exogenous prostaglandins.[5]

Clinical Features

The onset of the disease is usually acute.[4] The most commonly affected bone is the mandible affected in 90% of cases)[2] followed by the ulna, tibia, clavicle scapula and the ribs.[1] Occasionally, frontal and parietal bones, ilium and metatarsals are involved but it is not known to affect the phalanges or the vertebrae.[1] The involvement of more than one bone is common and the bilateral affection is often asymmetrical.[1]

Soft tissue swelling along the diaphysis of long bones that is deep seated, firm and freely mobile usually precedes the radiological changes.[4] Tenderness, fever and swelling have usually regressed by the time when radiologic changes become apparent.[1]

The course is protracted with remissions and exacerbations.[4] The clinical course is variable and unpredictable but the acute symptoms usually resolve over the course of a few months. The outcome is generally good with spontaneous resolution of the lesion but has been described after the initial episode.[6]

Laboratory Findings

The laboratoty examination may reveal an increased ESR, leucocytosis, thrombocythemia, increased alkaline phosphatase, increased immunoglobulin levels, increased C-reactive protein and anaemia.[6] Fever and ESR are thought to be related to the number of bones involved.[2]

Pathology

Biopsy of affected areas shows fibrinoid degeneration in hyperostotic bone and hyperplastic collagen fibres.[6] In the early stage, the bone is coarse and the underlying cortex is visible.[1] There is a marked inflammatory process involving the periosteum and adjacent soft tissues which gradually subsides, leaving the thickened periosteum and subperiosteal immature lamellar bone.[3] A vascular fibrous tissue occupies the bone marrow space.[3] Biopsy of the mature bony lesion reveals hyperplasia of the lamellar cortical bone.[3] In the long bones hyperostosis is confined to diaphysis sparing the metaphysic and epiphysis.[1]

Radiological Findings

Radiographic changes take 15 to 20 days to develop with hyperostosis being seen with well defined and stratified border.[2] There is formation of periosteal new bone in a laminated (onion peel) fashion, engulfing the diaphysis associated with soft tissue swelling.[3] Periosteal new bone at first exhibits a vague opacity gradually increases in density and then blends and thickens the cortex.[4] Distribution is patchy and asymmetrical and usually multifocal.[6]

MRI is an excellent modality of imaging but has no additional value in clinical management.[3]

Differential Diagnosis

Differential diagnosis of caffey disease includes osteomyelitis, child abuse, congenital syphyllis, hypervitaminosis A, scurvy, Ewing's sarcoma and metastatic neurofibroma.

In osteomyelitis, there is often a high grade fever and involvement of a single bone. Destruction of bone accompanies surrounding reactive bone formation. Usually bacteria can be cultured from the lesion and antibiotics are frequently effective.[4]

Ewing's tumor is similar in appearance because of its typical onion-peel laminations of subperiosteal ossification and because of the accompanying constitutional symptoms. There is central destruction on histology and marrow signal changes in MRI study.[4]

The subperiosteal hemorrhage following a contusion or incomplete fracture will often ossify. The lesion is confined to one bone and resolves without recurrence.[4]

Hypervitaminosis A occurs in infants over 12 months of age where mandible is never involved. Child is afrible and there is high level of Vitamin A.[4] Subperiosteal ossification is similar to Caffey disease in scurvy but ground glass appearance in all the bones is characteristic.[4]

Treatment

There is no specific treatment for caffey diasease.[1] Corticosteroids are effective in alleviating acute systemic manifestations but do not change the lesions.[3] NSAIDs can be used to treat child with recurrent Caffey disease.[3]

Surgery is performed to address the problems of synostosis, radial head dislocation and limb length inequality if they are symptomatic.[3]

Conclusion

Caffey disease is a rare self limiting condition that requires a high index of suspicion. It is usually confused with other conditions like osteomyelitis, Ewings sarcoma. Supportive and symptomatic treatment is the mainstay of treatment.

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