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Critical role of STIR MRI in early detection of post-streptococcal periostitis with dysproteinaemia (Goldbloom's syndrome)

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ABSTRACT

Objective. *In 1966, Goldbloom et al. described two children who developed a peculiar clinical picture characterised by intermittent daily bone pain in the lower limbs, fever spikes, increased acute phase reactants and dysproteinaemia. The syndrome occurred two weeks after a group A β-haemolytic streptococcus infection. So far, only a few cases have been reported in the medical literature in English.*

Methods. *We report two further cases of Goldbloom's syndrome with a review of the literature in English.*

Results. *Our two patients lived in the same Italian region and presented their syndrome onset a week apart. Early use of STIR MRI revealed an atypical metaphyseal hyperintensity in the femurs and tibias. X-ray showed periosteal hyperostosis. A short cycle of corticosteroids led to rapid recovery of symptoms and disappearance of bone changes.*

Conclusion. *The reported cases highlight a likely under-recognised post-streptococcal inflammatory periosteal reaction and emphasise the diagnostic utility of the newer imaging modalities.*

In 1966, Goldbloom *et al.* described two children who developed a peculiar clinical picture after a group A β-haemolytic streptococcus (GAS) infection, characterised by: (i) intermittent daily bone pain in the lower limbs with fever spikes, (ii) normal physical examination, (iii) increased acute phase reactants with atypical dysproteinaemia (hypoalbuminaemia and increased α1, α2 and γ globulinaemia), (iv) radiographic periosteal hyperostosis, (v) no malignancy at bone marrow biopsy and (vi) self-limited course (1). So far, this condition is largely unknown and only a few cases have been reported in the medical literature in English (2-6). Herein, we report two further cases, stressing on their early STIR (Short Tau Inversion Recovery) MRI (SM) features.

Patient 1 was a previously healthy 9-year-old girl who experienced intermittent daily bone pain in the lower limbs, associated with fever spikes (up to 40°C), limping and nocturnal awakenings. No history of trauma was reported. Only partial response to ibuprofen was observed. Physical examination was unremarkable. Laboratory tests showed mild anaemia (Hb 8 g/dl), thrombocytosis (PLT 680000/mmc), normal leucocyte count (11500/mmc), increased acute phase reactants (ERS 75 mm/h, CRP 7 mg/dl), and high antibody titre against streptolysin O (4280 UI/ml) and DNase-B (6310 UI/ml): an atypical dysproteinaemia, characterised by hypoalbuminaemia (2.8 g/dl) and increased α1, α2 and γ globulinaemia (respectively 0.7, 1.3, and 1.8 g/dl), was also noted. Throat swab was positive for GAS. Cardiologic and neurological examinations were both normal. X-ray of the lower limbs showed periosteal hyperostosis at the femurs and tibias (Fig. 1). On SM, these bones revealed hyperintense signal at the metaphysis (see Figure). On surgical biopsy, the periosteum appeared thickened and strongly adherent to the underlying bone. Histopathological examination showed signs of chronic inflammation. Two mg/kg/day prednisone was started, leading to complete recovery within three days. Therapy was regularly reduced after two weeks when all the laboratory tests were normal (Hb 14 g/dl, PLT 370000/mmc, WBC 8600/mmc, ERS 9 mm/h, CRP 0.4 mg/dl) and, finally, suspended after a month when the bone changes disappeared (Fig. 1)). No recurrence has been observed in the following years.

Patient 2 was a 6-year-old girl who developed daily attacks of severe bone pain with fever spikes (up to 41°C), two weeks after an untreated febrile pharyngitis. Joint examination did not show signs of active arthritis. Laboratory tests revealed high inflammatory markers (ERS 85 mm/h, CRP 17 mg/dl) and increased antibody titre against streptolysin O (1010 IU/ml) and DNase-B (1201 IU/ml). Throat swab was positive for GAS. Amoxicillin was given without benefit. In the following weeks, the patient experienced a profound weight loss and, then, hospitalised. Mild anaemia (Hb 9 g/dl), thrombocytosis (PLT 624000/mmc), normal leucocyte count (12000/mmc) and atypical dysproteinaemia with hypoalbuminaemia (3.5 g/dl) with increased α1, α2 and γ globulinaemia (respectively 0.7, 1.3, and 1.7

Table. Main features of our patients with Goldbloom's syndrome with review of the English literature.

	Patient 1	Patient 2	English literature (7 patients)
Gender	F	F	M:F=3:4
Mean age at onset (years)	9	6	8 (0.3-14)
Previous infection	pharyngitis	pharyngitis	pharyngitis (4), scarlet fever (1), otitis (1)
Intermittent daily bone pain with fever	yes	yes	all
Weight loss	no	yes	4 (57%)
Increased inflammatory markers	yes	yes	6 (86%)
Thrombocytosis	yes	yes	NA
Dysproteinemia	yes	yes	all
Positive throat swab culture for GAS	yes	yes	NA
Increased ASO titre	yes	yes	1 (14%)
Increased ADN-B titre	yes	yes	NA
Periosteal hyperostosis	yes	yes	all
Hyperintense bone areas on S-MRI	yes	yes	NA
Inflammation on bone marrow biopsy	yes	yes	3 (43%)
Response to oral prednisone	yes	yes	NA
Clinical resolution (months)	3 days*	2 days*	10 (0.5 – 12)
Laboratory resolution (months)	0.5*	0.5*	26 (4 – 66)
Radiological resolution (months)	1*	1*	33 (4 – 66)
Follow-up (months)	26	24	NA

NA: not available; *from prednisone administration.

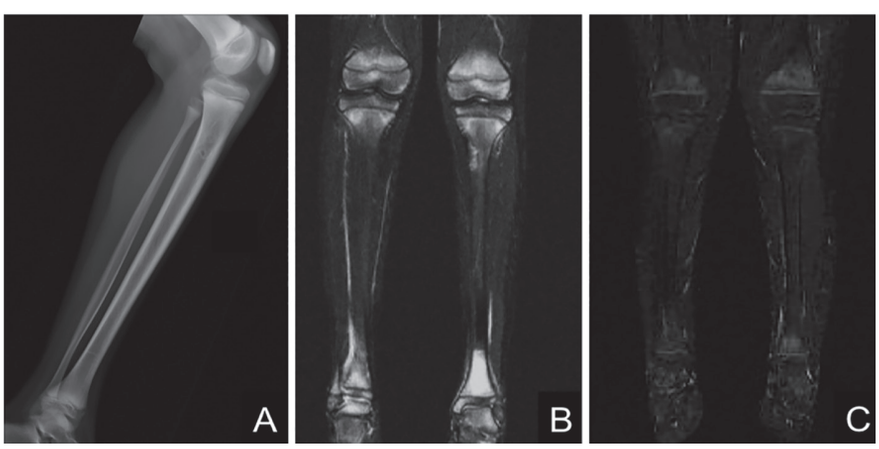

Fig. 1. Periosteal hyperostosis of the left tibia on x-ray (**A**) and metaphyseal hyperintensity of the femurs and tibias on STIR MRI first (**B**) and after (**C**) one month of corticosteroid therapy.

g/dl), were documented. SM showed metaphyseal hyperintensity in the femurs and tibias. Bone marrow biopsy showed signs of chronic inflammation. Two weeks of two mg/kg/die prednisone led to a prompt resolution of symptoms, accompanied by changing of haematological values to the normal range (Hb 13 g/dl, PLT 324000/mmc, WBC 8600/mmc, ERS 9 mm/h, CRP 0.5 mg/dl). No inflammatory signs were present on SM after one month. She was in good health two years after disease onset.

The clinical picture observed in our patients was consistent with the syndrome originally described by Goldbloom *et al*. One of the most striking features is the association with an infectious trigger, most often a GAS (1-4), as was seen in our cases. Interestingly, both our patients lived in the same Italian region (Lombardy) and presented the syndrome onset a week apart, suggesting that a particular strain of GAS could be responsible for their condition. No other cases of Goldbloom's syndrome have been notified to the Italian National Health Institute in that period (personal communication from Dr Roberta Creti, Department of Infectious, Parasitic and Immune-mediated Disease of the Italian National Health Institute).

Another peculiar aspect of this picture is the pattern of bone involvement. A severe periostitis represents the radiological hallmark and is responsible for the bone pain attacks. This feature could be underestimated in the past, particularly in the earlier stages, because of the exclusive use of standard x–ray. Nowadays, it is conceivable that the larger use of SM may offer a more sensitive diagnostic tool for the early detection of this condition.

Beside neoplastic and infectious bone diseases, other inflammatory diseases (*e.g*. chronic multifocal recurrent osteomyelitis and SAPHO) should be considered in the differential diagnosis of Goldbloom's syndrome, and late manifestations of Caffey's disease have also to be excluded. However, the typical clinical presentation with sudden disease onset, following a recent GAS infection, the presence of atypical dysproteinaemia, and the mono-phasic disease course represent characteristic features of this clinical entity that we propose to name post-streptococcal periostitis with dysproteinaemia (PSPD).

In conclusion, the reported cases highlight a likely under-recognised post-streptococcal inflammatory periosteal reaction and emphasise the diagnostic utility of the newer imaging modalities, namely SM. A timely diagnosis and a short cycle of corticosteroid may lead to rapid recovery of symptoms and disappearance of bone changes.

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