# Osseous presentation of Hodgkin's disease: a case report and review of the literature

R. Doğan Köseoğlu[1], Atilla Şenaylı[2], Ünal Bıçakçı[2], Nurper Onuk-Filiz[1]
Taner Sezer[3], Tiraje Celkan[4]

*Departments of [1]Pathology, [2]Pediatric Surgery, and [3]Pediatrics, Gaziosmanpaşa University Faculty of Medicine, Tokat, and [4]Department of Pediatrics, İstanbul University, İstanbul Faculty of Medicine, İstanbul, Turkey*

**SUMMARY: Köseoğlu RD, Şenaylı A, Bıçakçı Ü, Onuk-Filiz N, Sezer T, Celkan T. Osseous presentation of Hodgkin's disease: a case report and review of the literature. Turk J Pediatr 2007; 49: 218-222.**

**The bone involvement in the later stages of Hodgkin's disease is an expected phenomenon, but it is very rare in early stages of the disease. About 49 cases of Hodgkin's disease presenting with bone involvement have been reported in the literature. We reported a 14-year-old boy initially evaluated with pain localized at the left ilium. Although all the radiological examinations suggested an osseous anomaly, histopathologic evaluation of the pelvic lymphadenopathies provided definite diagnosis of the disease. We discuss the possible differential diseases and review the literature regarding the osseous presentation of Hodgkin's disease.**

***Key words:*** *Hodgkin's disease, osseous presentation.*

Hodgkin's disease usually presents with lymph node or solid organ involvement, but bone is another possible origin of the disease. In the literature, to our knowledge, only 49 cases of Hodgkin's disease with bone involvement at the very beginning of the disease have been reported, though bone involvement becomes increasingly prevalent at the later stages[1,2]. Here, we report a case of Hodgkin's disease presenting with bone involvement in a 14-year-old boy.

## Case Report

A 14-year-old boy was referred to the Pediatric Surgery Department of Gaziosmanpasa University Hospital with paroxysmal pain and growing mass in his left hip for two months. There was no family history of lymphoma or another tumor disease. He had no systemic symptoms or weight loss. In the physical examination, there was no lymphadenopathy or any mass palpated on the body except in the left iliac region. Blood chemistry studies were unremarkable, except for sedimentation rate of 81 mm per hour. X-ray and computerized tomography (CT) scan of the pelvis showed a destruction in the left ilium with a soft mass protruding through the pelvis. Also, in the para-aortic region, multiple lymphadenopathies were detected in CT scan. Technetium scintigraphy revealed hyperemic lesions with lytic and sclerotic areas in ilium.

Frozen examination of bone biopsy performed during the operation was not diagnostic and showed nonspecific inflammatory cell infiltration with extensive myxoid stromal changes and mesenchymal cells in atypical appearance supporting a soft tissue tumor in the iliac bone. Because of the nonspecific diagnosis in frozen examination, the operation was continued to excise the lymph nodes from the pelvic and para-aortic region. Histopathological examination of lymph nodes revealed polymorphic inflammatory cell infiltration separated by fibrous bands. Inflammatory infiltration was composed of reactive lymphocytes, eosinophils, and plasmocytes. In this reactive cellular background, scattered multilobulated and mononuclear Reed-Sternberg cells and lacunary cells were detected (Fig. 1). Reactive cell infiltration and Reed-Sternberg cells were also observed in bone biopsy (Fig. 1). The monoclonal antibodies against CD30, CD15 (LeuM1), CD3, CD20,

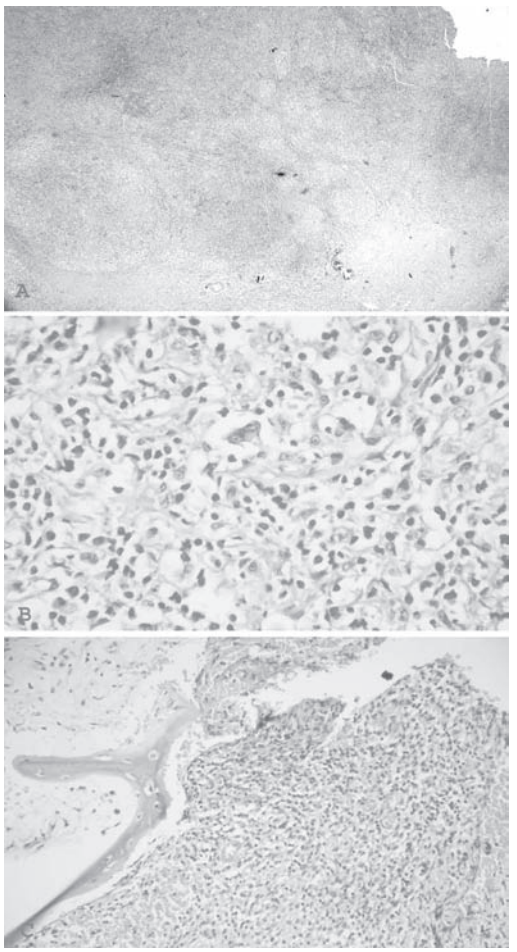

**Fig. 1.** A: Lymph node demonstrates effacement of the nodal architecture by cellular infiltrate (hematoxylin & eosin-HE, x10). B: The cellular infiltration consisting of mixed inflammatory cells and Reed-Sternberg cells in lymph node (HE, x40). C: Bone biopsy demonstrating a destructive cellular infiltrate (HE, x20).

and CD45 in both lymph node and bone tissue were used for immunohistochemical analysis. Reed-Sternberg cells showed positive staining for CD30 and CD15; cells were negative for CD45, CD3 and CD20. Histopathological and immunohistochemical features of lymph nodes and iliac bone were concordant with Hodgkin's disease, nodular sclerosis type.

The patient has been treated with adriamycin, bleomycin, vinblastine, dacarbazine (ABVD) chemotherapy for one year. In addition, radiotherapy has been performed for the last three months. The bone lesion regressed and lymphadenopathy was not present in the last follow-up. In the last physical examination, general condition of the patient was good and the patient was in remission.

## Discussion

Bone involvement in Hodgkin's disease occurs in 9% to 35% of the cases. The bone involvement is seen particularly in the later stages, but very rarely at the time of presentation[1-4]. In the literature, 49 cases of Hodgkin's disease with bone involvement were reported at the time of initial diagnosis (Table I). The majority of these cases also had lymph nodes and other organ involvement with bone lesions at staging workup. Age of these cases ranged from 5 to 85 years and the average age was 37.6 years; most cases were adults. Seven cases were determined in the age range of 5-15 years, not including our case. Twenty-six (53%) of the cases were male and 23 (47%) were female. The bones most involved at the initial diagnosis were vertebrae, pelvic bones, femur, humerus, sternum, tibia, scapula, mandible and rib.

In Hodgkin's disease, radiographic evidence of bone involvement is seen in 10-15% of cases[1]. The bone lesions of Hodgkin's disease may be lytic, sclerotic or mixed. Lytic lesions are more common than sclerotic lesions. As the bone involvement may be via hematogenous or direct invasion, the type of spreading can be related with the type of bone lesion. Lytic lesions usually support hematogenous dissemination, whereas sclerotic lesions support direct invasion from adjacent lymph nodes[5]. In the literature, radiological examinations revealing bone involvement at the initial diagnosis were present for 32 of 49 cases. Fifteen of 32 cases (46.8%) had lytic, nine cases (28.1%) had sclerotic, and three cases (9.4%) had mixed lesions. One case (3.1%) had periosteal reaction in his X-ray examination. Radiographs of four cases (12.5%) were normal. Radiological features of lesions were not reported for 17 of 49 cases. In the retrospective study of Ostrowski et al.[1], although the radiological features of the cases were analyzed, the details were not given individually. They reported in their series that osteolytic, osteosclerotic and mixed lesions were present in 24%, 24% and 46% of the cases, respectively[1].

The histopathological diagnosis could be obtained in only 22 of 49 cases. Ten of them were nodular sclerosis type Hodgkin's disease and nine cases were diagnosed as mixed cellular type Hodgkin's disease. Only three cases were reported as lymphocyte depletion type Hodgkin's disease. Histological subtypes of

**Table I.** List of the 50 Patients Reported in the Literature

| Case | Year | Age/ Gender | Involved bones at presentation | Other sites | Hodgkin subtype | Radiological feature | Ref. |
|---|---|---|---|---|---|---|---|
| 1 | 1927 | 42/M | T4–T8 vertebrae | – | unknown | unknown | 1 |
| 2 | 1958 | 53/M | Left humerus, Left ilium | – | unknown | unknown | 1 |
| 3 | 1934 | 58/M | Manubrium | Anterior chest wall soft tissue | unknown | unknown | 1 |
| 4 | 1953 | 50/M | Sternum | Bilateral axillary lymph nodes | unknown | unknown | 1 |
| 5 | 1967 | 30/M | Left tibia | Bilateral cervical lymph nodes | unknown | unknown | 1 |
| 6 | 1971 | 37/M | Right scapula | Right axillary lymph nodes | unknown | unknown | 1 |
| 7 | 1980 | 21/M | Left iliac crest, right sacrum | Para–aortic and pancreatic lymph nodes, T3, T10, L4 vertebrae | unknown | unknown | 1 |
| 8 | 1983 | 32/M | Right femur | Left supraclavicular lymph node, mediastinum | unknown | unknown | 1 |
| 9 | 1986 | 29/F | Right acetabulum, right humerus | Mediastinum, right supraclavicular lymph node | unknown | unknown | 1 |
| 10 | 1986 | 41/M | Right ribs | Right chest wall, intercostal muscle | unknown | unknown | 1 |
| 11 | 1986 | 41/M | T10 vertebra | Lung, T4, T6, L1 vertebrae, cervical, inguinal, para–aortic lymph nodes, spleen | unknown | unknown | 1 |
| 12 | 1991 | 13/M | L1,L4 vertebrae | Mediastinum, lung | unknown | unknown | 1 |
| 13 | 1993 | 51/F | Right ilium | Mediastinum | unknown | unknown | 1 |
| 14 | 1996 | 11/M | Left ilium | Cervical lymph nodes, mediastinum, liver, left ischium, right femur | unknown | unknown | |
| 15 | 1960 | 73/F | Right femur | – | unknown | unknown | 1 |
| 16 | 1968 | 34/M | Left humerus | – | unknown | unknown | 1 |
| 17 | 1995 | 61/F | T11 vertebra | – | unknown | unknown | 1 |
| 18 | 1987 | 52/M | T8 vertebra | unknown | NS | Sclerotic | 9 |
| 19 | 1987 | 42/M | L5 vertebra | unknown | LD | Lytic | 9 |
| 20 | 1966 | 21/F | Sternum | Mammary | unknown | Sclerotic | 10 |
| 21 | 1972 | 45/M | Sternum | Right axilla | NS | Periosteal | 11 |
| 22 | 1987 | 22/F | Sternum | Mediastinum, right axilla | NS | Lytic | 12 |
| 23 | 1988 | 14/M | Sternum | Axillae | unknown | Lytic | 13 |
| 24 | 1988 | 19/F | Sternum | Mediastinum | NS | Lytic | 13 |
| 25 | 1943 | 5/F | Left scapula | None | unknown | Lytic | 14 |
| 26 | 1987 | 83/F | Clavicle | unknown | MC | Lytic | 9 |
| 27 | 1936 | 40/M | Left femur | unknown | unknown | Lytic | 15 |
| 28 | 1987 | 30/F | Femur | Axillae, para–aortic lymph nodes | MC | Lytic | 9 |
| 29 | 1936 | 24/F | Left femur | Inguinal lymph node | unknown | Lytic | 15 |
| 30 | 1943 | 27/F | Right tibia | Inguinal lymph node | unknown | Sclerotic | 14 |
| 31 | 1993 | 31/M | Sacrum | None | MC | Sclerotic | 4 |
| 32 | 1936 | 39/F | Left humerus | None | unknown | Lytic | 15 |
| 33 | 1982 | 12/M | Left femur | Spleen | MC | Lytic | 16 |
| 34 | 1979 | 25/F | Left humerus | None | unknown | Lytic | 17 |
| 35 | 1996 | 27/F | Right ilium | Parasacral lymph nodes | MC | Sclerotic | 5 |
| 36 | 1996 | 55/F | Left sacroiliac region | Cervical lymph nodes | NS | Sclerotic | 5 |
| 37 | 1996 | 68/F | Right ilium | Para–aortic, mesenteric lymph nodes | MC | Sclerotic | 5 |
| 38 | 1996 | 24/M | T12 vertebra | Anterior mediastinum, cervical lymph nodes | NS | Sclerotic | 5 |
| 39 | 1999 | 10/M | Right ischium | Spleen | unknown | Lytic | 3 |
| 40 | 1997 | 41/F | Left acetabulum, left femur neck | Inguinal lymph nodes, vertebra, pelvis | NS | Mixed | 6 |
| 41 | 1989 | 61/M | T11,L1,L5 vertebrae | Rib, right scapula, femur | NS | Sclerotic | 7 |
| 42 | 1997 | 60/F | Mandible | Liver, spleen, pleura | NS | Lytic | 2 |
| 43 | 1984 | 34/F | Mandible | Bone marrow, spleen | unknown | unknown | 18 |
| 44 | 1992 | 30/M | Sacrum | Abdominal lymph nodes | MC | Normal | 8 |
| 45 | 1992 | 19/F | Right ilium | Supraclavicular, inguinal lymph nodes | LD | Normal | 8 |
| 46 | 1992 | 34/F | T12,L2,L5 vertebrae, femur acetabulum | Inguinal, mediastinal, lumbo–aortic lymph nodes | MC | Normal | 8 |
| 47 | 1992 | 49/M | L4,L5 vertebrae | Supraclavicular, mediastinal, abdominal lymph nodes, extradural mass, liver | NS | Mixed | 8 |
| 48 | 1992 | 40/M | T10 vertebra, rib, knee | Right psoas muscle, retroperitoneal lymph nodes, bone marrow | LD | Normal | 8 |
| 49 | 1992 | 85/F | Pelvic bones | Mediastinal, abdominal lymph nodes, bone marrow | MC | Lytic | 8 |
| 50 | Pre–sent case | 15/M | Left ilium | Para–aortic, pelvic lymph nodes | NS | Mixed | 8 |

MC: Mixed cellular. LD: Lymphocyte depletion. NS: Nodular sclerosis.

Hodgkin's disease in 27 cases were not certain. Thus, nodular sclerosis and mixed cellular subtypes were determined at about equal proportions in the literature. We determined nodular sclerosis type Hodgkin's disease in our case.

The differential diagnosis of Hodgkin's disease presenting with primary or secondary bone involvement is very important. Anaplastic lymphoma or peripheral T-cell lymphoma may show similar histologic picture, but non-Hodgkin's osseous lymphomas, especially peripheral T-cell lymphomas, may cause fibrosis or sclerosis in bone marrow and bone. Furthermore, all these lymphomas also have a significant large cell component[5]. Another entity causing a similar diagnostic dilemma is malignant fibrous histiocytoma of the bone[1]. Osteomyelitis is an important disease in the differential diagnosis. Both clinical and radiological features of osteomyelitis are very similar to osseous Hodgkin's disease. In osteomyelitis, small biopsies are not helpful in the differential diagnosis. In the literature, we determined that many cases of Hodgkin's disease with bone involvement were diagnosed as osteomyelitis at the initial evaluation[1,2,5]. The other entities that should be regarded in the differential diagnosis are eosinophilic granuloma, chondrosarcoma, Paget's disease and primary sarcoma of bone[1-3,5].

Most of the cases previously reported in the literature were diagnosed before the utilization of immunohistochemical studies. Therefore, diagnosis of Hodgkin's disease may be suspect in these cases. The immunophenotypes of Reed-Sternberg cells and variants are similar for nodular sclerosis, mixed cellular and lymphocyte-depletion types. Nodular sclerosis is the most frequent histological type in Hodgkin's disease with bone involvement, followed by mixed cellular type. For these reasons, immunohistochemical analysis should be performed to eliminate other diagnostic possibilities and to confirm the diagnosis of bone-involving Hodgkin's disease[5].

Whenever malignant lymphoid cell infiltration is determined in bone, it is important to decide whether this infiltration is primary or secondary. Primary lymphoma of bone is extremely rare. It constitutes 3-8% of primary malignant bone tumors. Most of the primary bone lymphomas are non-Hodgkin's lymphomas; primary Hodgkin's disease of bone is seldom encountered[1,5]. In the reviewed literature, only seven cases had been reported as primary osseous Hodgkin's disease[1,2,7]. Four of these cases had been reported before 1970[1]. Therefore, the diagnosis of these cases should be cautiously regarded due to inadequate clinical evaluation and staging procedures in the past. No organ or lymph node involvement within six months from initial diagnosis must be determined for the diagnosis of "primary osseous Hodgkin's disease"[1].

As the chemotherapy in Hodgkin's disease with bone involvement has an important effect on the prognosis, survival is better than expected[1,5].

Here, we report Hodgkin's disease presenting with bone involvement in a 14-year-old boy who had pain complaint in his left hip region for two months. In the preoperative period, the case was interpreted as primary bone tumor based on clinical and radiological evaluation. Intraoperative frozen study of iliac bone biopsy was not diagnostic. The diagnosis could be reached by histopathological investigation of pelvic and para-aortic lymph nodes. In the histopathological examination, nodular sclerosis type Hodgkin's disease was determined in our case. Radiological bone lesions of Hodgkin's disease are mostly lytic in character but they may also be sclerotic or mixed. Radiological findings of bone lesions were mixed in our case. Therefore, Hodgkin's disease should be remembered in the differential diagnosis of lytic lesions involving especially vertebrae and pelvic bones.

**REFERENCES**

1. Ostrowski ML, Inwards CY, Strickler JH, et al. Osseous Hodgkin's disease. Cancer 1999; 5: 1166-1178.
2. Jamshed A, Allard WF, Mourad WA, et al. Primary Hodgkin's disease of the mandible: a case report and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997; 83: 680-684.
3. Mehta R, Gupta A, Dewan S, et al. Hodgkin's disease presenting with bone involvement. Indian Pediatr 1999; 36: 925-927.
4. Borg MF, Chowdhury AD, Bhoopal S, et al. Bone involvement in Hodgkin's disease. Australas Radiol 1993; 37: 63-66.
5. Özdemirli M, Mankin HJ, Aisenberg AC, et al. Hodgkin's disease presenting as a solitary bone tumor: a report of four cases and review of the literature. Cancer 1996; 1: 79-88.

6. Sekinel I, Sasaki Y, Hasebe T, et al. Coxalgia as the initial symptom in Hodgkin's disease: a case report. Jpn J Clin Oncol 1997; 27: 353–356.
7. MacCormick R, Covert A, Gross M. Primary bony involvement in Hodgkin's disease. CMAJ 1989; 140: 1059-1060.
8. Gaudin P, Juvin R, Rozand Y, et al. Skeletal involvement as initial disease manifestation in Hodgkin's disease: a review of 6 cases. J Rheumatol 1992; 19: 146-152.
9. Vassallo J, Roessner A, Vollmer E, et al. Malignant lymphomas with primary bone manifestation. Pathol Res Pract 1987; 182: 381-389.
10. Arnold HS, Meese EH, D'Amoto NA, et al. Localized Hodgkin's disease presenting as a sternal tumor and treated by total sternectomy. Ann Thorac Surg 1966; 2: 87-93.
11. Meher-Homji DR, De Souza LJ, Mohanty B, Culcuttawalla XX. Unusual sternal mass in Hodgkin's disease. A case report. J Bone Joint Surg 1972; 54: 402-404.
12. Sullivan WT, Solonick DM. Case report 414. Skeletal Radiol 1987; 16: 166-169.
13. Manoli II A, Blaustein JC, Pedersen HE. Sternal Hodgkin's disease. Report of two cases. Clin Orthop 1988; 228: 20-25.
14. Kooreman PJ, Haex AJ. Hodgkin's disease of the skeleton. Acta Med Scand 1943; 115: 177-196.
15. Spencer J, Dresser R. Lymphoblastoma (Hodgkin's and sarcoma type) of bone. N Engl J Med 1936; 214: 877-879.
16. Chan KW, Rosen G, Miller DR, Tan CT. Hodgkin's disease in adolescents presenting as a primary bone lesion. A report of four cases and review of the literature. Am J Pediatr Haematol Oncol 1982; 4: 11-17.
17. Gold RH, Mirra JM. Case report 101. Skeletal Radiol 1979; 4: 233-235.
18. Cohen MA, Bender S, Struthers PJ. Hodgkin's disease of the jaws. Review of the literature and report of a case. Oral Surg Oral Med Oral Pathol 1984; 57: 413-417.