

## CASE REPORT

# A rare spindle-cell variant of non-Hodgkin's lymphoma of the mandible

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**ABSTRACT**

A 64-year-old male farmer presented with a rapidly progressive swelling of the left mandible since 6 months. The swelling was firm to hard, diffuse, nontender, obliterating the vestibule with paresthesia of lower lip. The cone beam computed tomography imaging revealed an ill-defined, moth-eaten radiolucency with destruction of the buccal and lingual cortical plates. The rapid growth and aggressive behavior of the lesion coupled with guidance from the patient's previous reports from the incisional biopsy and fine needle aspiration cytology warranted a mandibular resection. Microscopic examination showed an encapsulated lesion situated in the connective tissue containing a mixture of proliferating spindle-shaped cells arranged in fascicles and round cells infiltrating into the connective tissue stroma and bone. The neoplastic cells exhibited atypical features such as pleomorphism, hyperchromatism and increased mitotic figures with noncleaved nuclei. A working diagnosis of a spindle-cell sarcoma was arrived at with various differentials provided such as fibrosarcoma, rhabdomyosarcoma, leiomyosarcoma, malignant peripheral nerve sheath tumor, Langerhans cell histiocytosis and lymphoma and stating the need for immunohistochemistry to subtype the tumor. The neoplastic cells were negative for Van Gieson's stain and Masson's trichrome. Immunohistochemical analysis performed using desmin, smooth muscle actin, S-100 and CD1a in a bid to determine the phenotype of the tumor and rule out the previously stated differentials were all negative for the lesion. Lymphoid markers such as leukocyte common antigen and CD20 (cluster differentiation marker for B-cells) showed positivity in spindle-shaped cells as well as round cells indicating the tumor to be a lymphoproliferative lesion of B-cell type. A final diagnosis of "spindle-cell variant of non-Hodgkin's lymphoma" was rendered based on the immunohistochemical profile.

**Key words:** Immunohistochemistry, non-Hodgkin's lymphoma, spindle cells

**INTRODUCTION**

Lymphoma is a heterogeneous malignancy of the lymphatic system characterized by proliferation of lymphoid cells or their precursors. They are generally categorized as Hodgkin's and non-Hodgkin's lymphomas (NHLs) based on the presence and absence of typical Hodgkin's cells. Hodgkin's lymphoma rarely presents as extranodal disease, whereas NHL commonly presents at extranodal sites (25–45%) such as gastrointestinal

tract, skin and bone. In the head and neck, primary NHL occurs in Waldeyer's ring, oral mucosa, salivary glands, paranasal sinuses, laryngeal tissue and bone. The mandible accounts for only 0.6% of isolated NHLs. When it does occur, mandibular NHL closely mimics an ameloblastoma, a tumor of odontogenic epithelial origin, both clinically and radiographically.<sup>[1,2]</sup>

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Genetic diseases, environmental agents and infectious agents have been attributed to the development of NHL. Epstein–Barr virus, human T-cell lymphotropic virus 1, human immunodeficiency virus, *Helicobacter pylori*, chlamydia and human herpesvirus-8 are known to be associated with an increased risk of NHL. While the actual role of viruses in lymphomagenesis remains to be understood, some types of NHL have shown insertion of exogenous genes by oncogenic viruses.<sup>[3,4]</sup>

We present a rare case of rapidly progressing swelling of the left mandible which on routine histopathological examination appeared to be a spindle-cell sarcoma. Immunohistochemical analysis enabled a final diagnosis of spindle-cell variant of lymphoma, an occurrence previously reported only once in English literature.

## CASE REPORT

A 64-year-old male presented with a rapidly progressive swelling of the left mandible since 6 months for which he had undergone fine needle aspiration cytology and an incisional biopsy elsewhere with a diagnosis of benign mesenchymal neoplasm and chronic inflammatory granulation tissue, respectively.

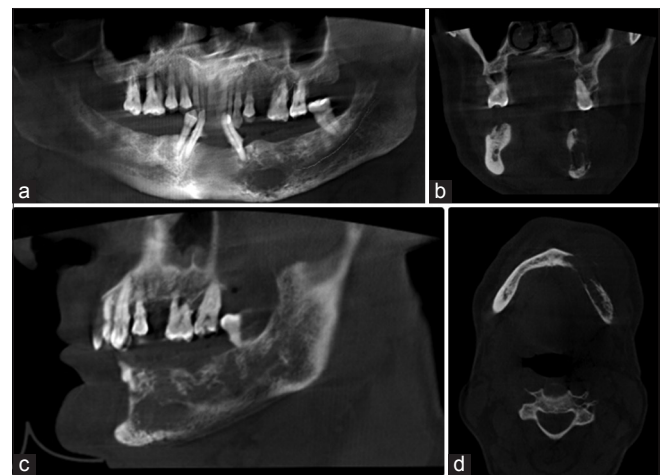
Extraoral clinical examination revealed a firm to hard diffuse soft tissue swelling measuring 4 cm × 5 cm that extended anteroposteriorly from midline to the left angle of the mandible and inferiorly extended 2 cm below the inferior border of the mandible [Figure 1a and b]. Intraorally, buccal cortical expansion was noted from midline to second molar region obliterating the vestibule with paresthesia of lower lip [Figure 1c]. Overlying skin and mucosa were intact with no ulcers or draining sinuses. The swelling was bony hard and nontender. A single lymph node measuring 1.5 cm was palpable in the left submandibular region.

Cone beam computed tomography (Planmeca ProMax<sup>®</sup>3D; Large FOV [200 mm × 100 mm]) imaging revealed an ill-defined, moth-eaten radiolucency in the left mandibular premolar/canine region with destruction of buccal and lingual cortical plates [Figure 2a-d]. No abnormality was seen in

the chest X-ray. Serum calcium, phosphorous, alkaline phosphatase and parathyroid hormone levels were within normal limits.

A clinically aggressive growth in the mandible with radiographic evidence of bone destruction entailed a differential diagnosis of ameloblastoma, malignant salivary gland tumor, aggressive osteomyelitis, malignant connective tissue neoplasm and metastasis from unknown primary, thereby warranting a mandibular resection.

Gross examination of the resected hemimandible showed attached lesional soft tissue measuring approximately “10.5 cm × 8.0 cm × 5.0 cm,” white to brown in color, with multiple cystic spaces and no “crackling” upon palpation [Figure 3a].

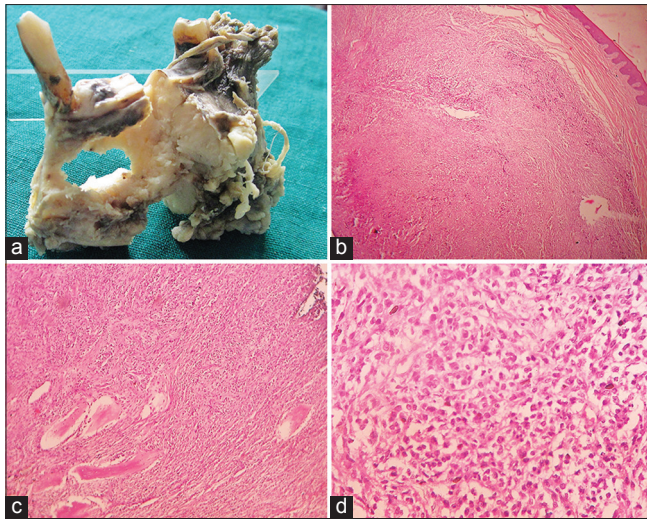


**Figure 2:** (a) Cone beam computed tomography reconstructed panoramic image showing diffuse radiolucency in the left body of mandible extending superiorly to the alveolar crest and inferiorly to lower border; anteriorly to apex of 33 and posteriorly till the region of 36. (b) Cone beam computed tomography coronal section showing radiolucent lesion in the left body of mandible extending through buccal and lingual cortex, minimal mucosal thickening of the right and left maxillary sinus floor is seen. (c) Cone beam computed tomography sagittal section revealed radiolucency extending from 33 to 38 with erosion of the mandibular nerve canal. (d) Cone beam computed tomography axial section showing asymmetry on left side with loss of buccal and lingual cortical plates and no evidence of expansion of the cortical plates



**Figure 1:** (a and b) Extraoral examination of left mandibular swelling that was firm to hard diffuse soft tissue swelling extending anteroposteriorly from midline to the left angle of the mandible and inferiorly extended 2 cm below the inferior border of the mandible. (c) Intraoral view showing the unilateral (left) involvement of the lesion





**Figure 3:** (a) Gross surgical specimen showing the erosion and perforation of the buccal and lingual cortical plates. Cut surface of the tumor showing lingual invasion below the inferior border of mandible. (b): Photomicrograph showing presence of mixture of spindle- and round-shaped cells arranged in fascicles separated from normal epithelium by grenz zone (H&E stain, x40). (c) Photomicrograph showing tumor cells infiltrating the bone (H&E stain x40). (d): Photomicrograph showing round to spindle shaped tumor cells with hyperchromatic nuclei (H&E stain, x400)

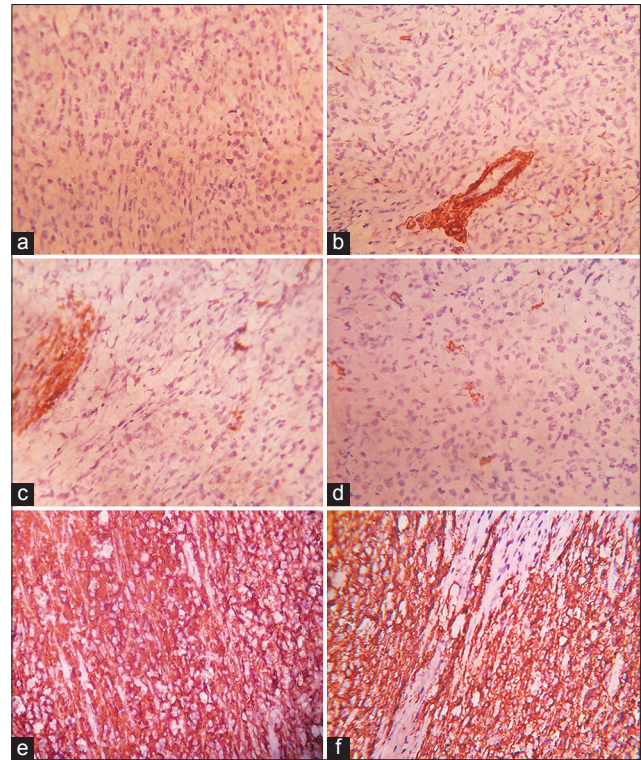
Microscopic examination showed an encapsulated lesion situated in the connective tissue and separated from the overlying normal epithelium by a grenz zone [Figure 3b]. Morphologically, the neoplastic tissue showed a mixture of proliferating spindle-shaped cells arranged in fascicles and round cells infiltrating into the connective tissue stroma and bone [Figure 3c]. The neoplastic cells exhibited atypical features such as pleomorphism, hyperchromatism and increased mitotic figures with noncleaved nuclei [Figure 3d].

Immunohistochemical staining with desmin [Figure 4a], smooth muscle actin (SMA) [Figure 4b], S-100 [Figure 4c] and CD1a [Figure 4d] were negative and lymphoid markers leukocyte common antigen (LCA) and CD20 (cluster differentiation marker for B-cells) showed positivity in spindle-shaped cells as well as round cells indicating the tumor to be a lymphoproliferative lesion of B-cell type [Figure 4e and f]. A final diagnosis of “spindle-cell variant of NHL” was rendered based on the immunohistochemical profile.

Postsurgical management of the patient was uneventful, and the disease was classified as Ann Arbor Stage IIE based on the involvement of the mandible and submandibular lymph nodes. The patient underwent chemotherapy vide the cyclophosphamide, adriamycin, vincristine and prednisolone regimen and has remained disease free for 12 months of follow-up.

## DISCUSSION

Lymphoma is a malignancy of the lymphatic system characterized by proliferation of lymphoid cells or their precursors with



**Figure 4:** Round- and spindle-shaped tumor cells showing negativity for (a) desmin (IHC stain, x400); (b) smooth muscle actin (internal positive control; vessel wall) (IHC stain, x400); (c) S-100 (internal positive control; nerve) (IHC stain, x400), (d) CD1a (IHC stain, x400). The cells were positive for (e); leukocyte common antigen (lymphoid lineage marker) (IHC stain, x200); and (f) CD20 (B-cell marker) (IHC stain, x200)

purely a round cell morphology. Morphologically, the present case posed a diagnostic challenge by exhibiting proliferating compact spindle and round cells arranged in short fascicles with focal areas showing storiform pattern that was suggestive of spindle-cell sarcoma. The spindle-shaped cells warrant distinction from other neoplasms with spindle-cell morphology. Special trichrome stains such as Van Gieson's stain and Masson's trichrome stains were performed and supplemented by immunohistochemistry to eliminate the possibility of collagenous tumors. Immunohistochemically, the tumor cells were negative for the desmin, SMA, S-100 and CD1a but strongly positive for LCA and CD20 suggesting a spindle-cell variant of lymphoma.

Hematolymphoid neoplasms with prominent spindle-cell features, also termed spindle-cell lymphoma, are rare but have been reported to occur in anaplastic large-cell lymphoma, “reticulum cell sarcoma,” primary bone lymphoma and primary soft tissue and/or skin lymphoma. Morphologically, these cases exhibit proliferation of spindle cells arranged in fascicles leading to a diagnosis of spindle-cell neoplasms of nonlymphoid origin.<sup>[5]</sup>

The origin of spindle-cell B-cell lymphomas is uncertain, with previous investigators (Ferrara *et al.*, 2002; Lim *et al.*, 2008; Yun 2009) reporting cases of spindle-cell B-cell lymphomas as variants of follicular lymphoma, whereas others (Wang

*et al.*, 2010; Kahlifa *et al.*, 2003; Ries *et al.*, 2007; Bhatia *et al.*, 2008) have classified them as a variant of diffuse large B-cell lymphoma.<sup>[1,6-8]</sup>

Kluin *et al.*<sup>[9]</sup> while reporting three cases of primary B-cell malignant lymphoma in the maxilla with sarcomatous pattern noted that the spindle cells in these cases did not represent the malignant lymphoid cells, but rather they were a fibrotic stromal response as well as cytoskeleton alterations to the tumor which is seen particularly in tumor invasion of bone and soft tissue. The present case however prominently displayed spindle-cell morphology amidst the lymphoid cell population (as proven with immunohistochemistry too), rather than in the surrounding stromal cells.

Cerroni (2002), in a reported case series of cutaneous spindle-cell B-cell lymphoma, stated that spindled nuclei likely correspond to centrocytes and to a lesser extent centroblasts of follicular center cell origin, whereas somewhat larger and more monomorphous spindle cells are consistent with a spindle-cell variant of diffuse large B-cell lymphoma.<sup>[7]</sup> A case of cutaneous spindle-cell B-cell lymphoma reported by Goodlad, 2001,<sup>[6]</sup> exhibited immunohistochemical expression of CD10 and Bcl-6 in addition to focal immunostaining of CD23 and CD35 for follicular dendritic cell networks within neoplastic follicles, prompting them to propose a follicular center cell origin.

Carbone *et al.* reported five cases of spindle-cell B-cell lymphoma and based on immunohistochemical studies, genetic analysis and clinical presentation, categorized them as a variant of diffuse large B-cell lymphoma. All five cases exhibited immunoreactivity for B-cell markers (CD20, CD79a) and Bcl-6 but were negative for T-cell markers (CD3 and CD5), CD10 and MUM-1. Furthermore, the finding of somatic immunoglobulin and Bcl-6 mutations favor the origin of this lesion from B-cells in an early phase of intragerminal center maturation. In addition, all cases showed the absence of chromosomal translocation t(14;18) that is otherwise characteristic of follicular lymphoma.<sup>[10]</sup>

Fung *et al.* (1993) and Wang *et al.* (2010) reported cases which showed positivity for SMA and believed that the spindling probably results from aberrations in the cytoskeleton; however, the tumor cells were negative for SMA in the present case.<sup>[8,10,11]</sup>

It has been hypothesized that cytokines such as tumor necrosis factor alpha, platelet-derived growth factor and transforming growth factor beta are produced by tumor cells which induce proliferation of fibroblasts in turn causing spindle-cell deformation within lymphoma cells.<sup>[12]</sup>

The differential diagnosis of spindle-cell tumors does not normally include malignant lymphoma, a neoplasm that commonly has small round-cell morphology. While the spindle-cell B-cell lymphoma has previously been commonly reported to occur within the skin, particularly of the head, neck and back regions, the current case illustrates that on rare occasions, the spindle

variant of B-cell NHL may present in the mandible, an occurrence previously only reported by Chi *et al.*, (2012).<sup>[1]</sup>

The prognosis of NHL depends mainly on the histology and the stage of the tumor (whether it is localized or not, stage of evolution, number of extranodal localizations, etc.). The location of the tumor (e.g. presenting in the jaw) is not found to be a significant prognostic factor as yet.<sup>[13]</sup>

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### Conflicts of interest

There are no conflicts of interest.

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