TJC Turkish Journal of Cancer
Volume 38, No. 1, 2008

Images in hematology-oncology

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Cytologic diagnosis of a lesion at the periphery of the lung

A 32-year old male was admitted to a regional state hospital due to intractable back pain which woke him up during sleep and showed slow progression over few months. Plain chest film was taken and anti-analgesics were prescribed. His complaints did not pass or regress and a thorax computerized tomography (CT) scan was done. A mass lesion, base of which was resting on the pleural surface with dimensions of 4x3 cm was located at the superior segment of the lower lobe of the right lung. The lesion was also slightly eroding the neighboring ribs. With all the data indicating a probable lung lesion, he was admitted to our faculty for the operation.

Due to pre-diagnosis of an adenocarcinoma, a bronchoscopy was performed and bronchioloalveolar lavage was taken. Bronchoscopy revealed no endobronchial lesion and lavage was found negative for malignancy. Preoperative Fine-needle aspiration biopsy was performed as an outpatient procedure at the radiology department under the guidance of CT where a pathologist was there to assess the sufficiency of the aspirated material. Three passes were done and most of the slides were fixed in alcohol for Papanicolau (PAP) staining, some air dried for modified May-Grünwald-Giemsa (MGM) stain. Additionally, 3 cell blocks were prepared, to apply possible ancillary techniques if required.

The microscopic evaluation of the slides revealed florid proliferation of epitheloid cells some with large finely vacuolated cytoplasm hence with a preserved nucleus/cytoplasmic (N/C) ratio, and some with less abundant cytoplasm with higher N/C ratio, slightly hyperchromatic nuclei with irregular nuclear membranes, some with conspicuous nucleoli and binucleation (Figure 1). The background was rich in chondromyxoid substance where in MGM showed metachromatic staining (Figure 2). There were no mitosis or necrosis and/or bizarre nuclei. Therefore, ancillary techniques (cytochemical and immunocytochemical) were applied to cell blocks. The tumor cells were mucicarmen, Pan-keratin and calretinin negative; and showed strong cytoplasmic positivity for vimentin (Figure 3) and S-100 protein (Figure 4). Ki-67 revealed nuclear positivity in 7/50 cells counted in high power field (HPF).

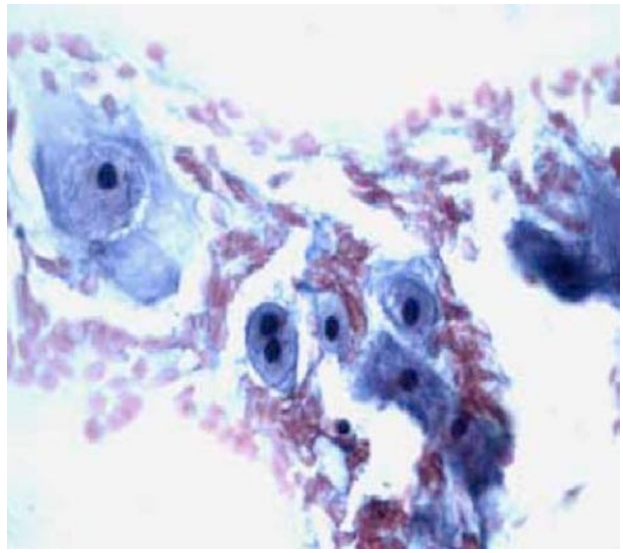

Fig 1. Tumor cells showing hyperchromatic nuclei, binucleation and abundant finely vacuolated cytoplasm (PAP, x400)

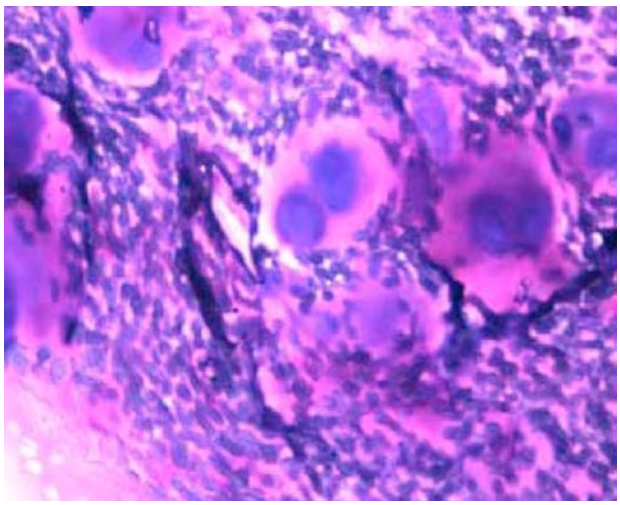

Fig 2. Abundant chondromyxoid matrix in the background (MGM, x200)

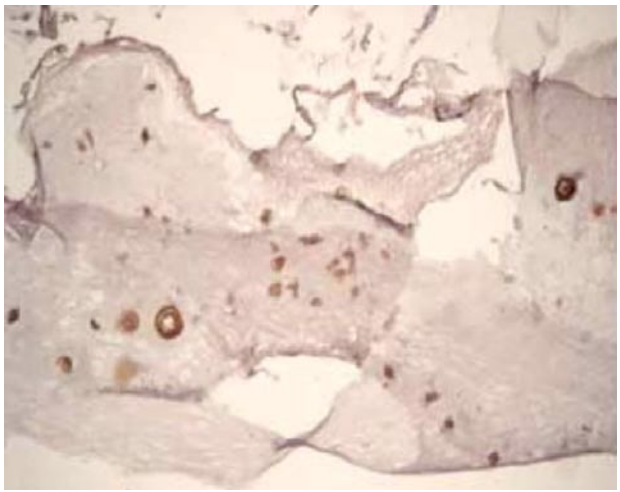

Fig 3. Cytoplasmic vimentin positivity in tumor cells, cell block (x400)

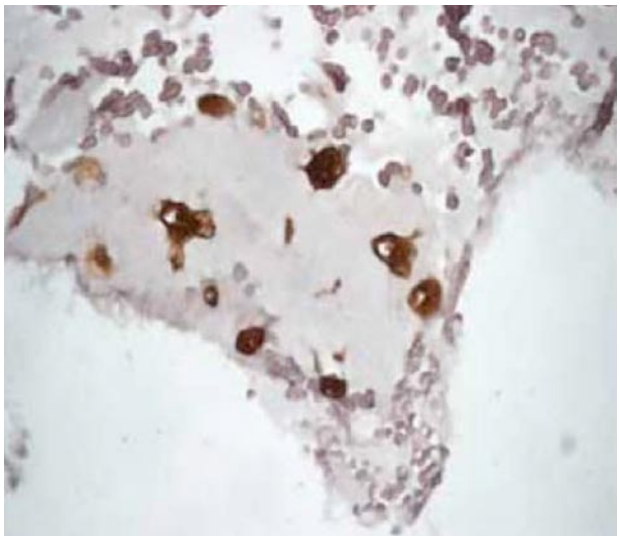

Fig 4. Cytoplasmic S-100 protein positivity in tumor cells, cell block (x400)

What is your diagnosis?

DIAGNOSIS

With all the cytomorphologic features and the cyto-/immunocyto-chemical staining characteristics, diagnosis of "tumor with chondroid differentiation suggestive of a chondrosarcoma (low grade)" was rendered.

After the exclusion of an adenocarcinoma of the lung and/or mesothelioma but the establishment of chondrosarcoma, radiologic investigations were further carried out with a second CT, Magnetic Resonance Imaging (MRI) of the thorax and Positron Emission Tomography (PET). The CT with a better quality of imaging together with MRI, revealed that the lesion was consistent with a primary bone tumor (probably originating from the 6th rib) and with infiltration to 5-6th neural foramen. PET result was in favor of a minimally hypermetabolic mass, FDG content of which was not high enough to demonstrate a malignancy, but also, could not exclude a low grade malignancy with low metabolic activity.

In the light of all the data in hand, a neurosurgeon was also included in the operative team of thoracic surgeons and the patient underwent thoracotomy, without confirmation of a preoperative tissue biopsy or intraoperative pathologic consultation (frozen section). The lesion was completely excised with partial excision of the 5-6th ribs and 6th vertebra. The histologic examination of the tumor was consistent with conventional type chondrosarcoma-grade II (Figure 5), located on the costal convexity of 6th rib, showing multifocal infiltration within the pleura and focal invasion of the intramedullary space. Ki-67 score of the resected tumor varied from 0-38% in different areas of the sections (Figure 6).

DISCUSSION

Chondrosarcomas are rare primary tumors of the bone, being the third most frequent (approximately 20% of all malignant tumors of the bone) (1-3). They are mostly seen in adulthood and old age. The tumor is commonly located in large bones of the axial skeleton (ilium), poximal humeri and femur or ribs (2-4). Male to female ratio is 1.5:1 (4). Most common presenting symptom is pain which is more severe at nights and it could last for months to decades owing to the slow progression of the tumor (3,4). Chondrosarcoma has an affinity for central skeleton and for the metaphysis or diaphysis of the affected bone (4). Usually the cortex, above the tumor is thickened, but

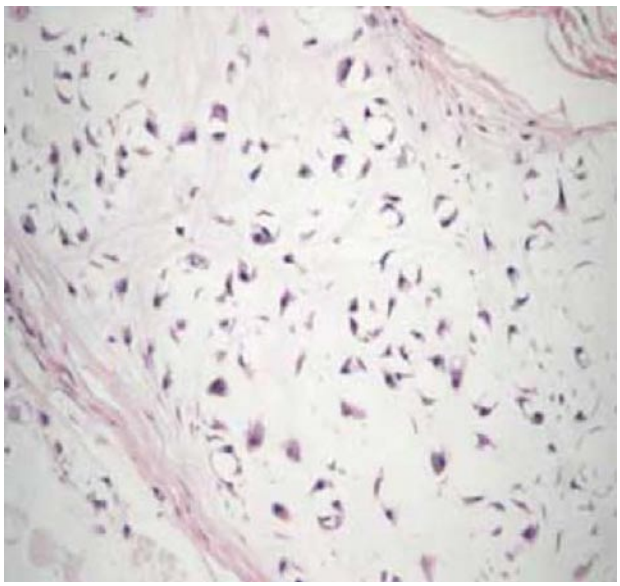

Fig 5. Histologic section of the resected tumor (H&E, x200)

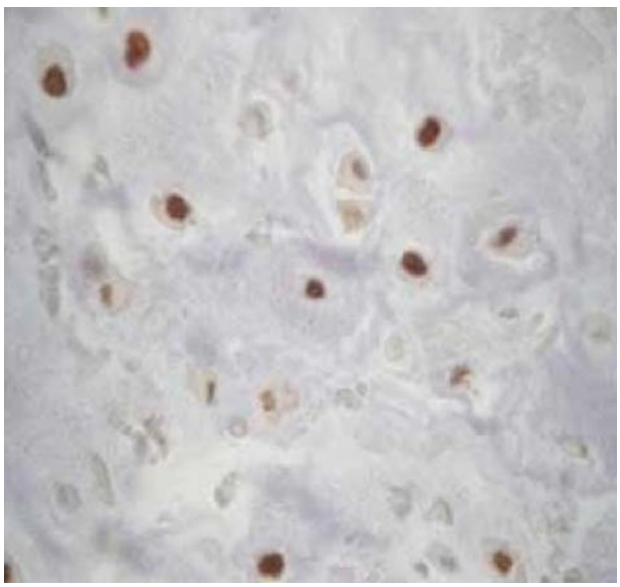

Fig 6. Ki-67 nuclear positivity in tumor cells in the histologic section (x400)

in high grade tumors a permeative growth pattern with destruction of bone is a characteristic radiologic finding (3,4).

Cytology of the chondrosarcomas -especially the low grade ones- are extremely challenging. Therefore, owing to the rarity of the chondrosarcomas, most of the practicing cytopathologists may not encounter such bone tumors, hence comparatively may lack the experience to grade such tumors cytologically. On the other hand, close scrutiny of the aspirated material with special attention given to the parameters such as cellularity, nuclear size and shape, double or multiple nuclei, presence or absence of macronucleoli, cytoplasmic features, presence or absence of necrosis and mitosis may lead to correct grading of the chondrosarcomas, at least as low or high grade; if not an exact histologic diagnosis of the grade as I, II, III or IV (1,5,6).

Cytology of chondrosarcomas may be quite confusing not only when chondroid lesions or tumors with chondroid differentiation are concerned, but also with some other tumors of different histologic types, like chordoma or even mucinous adenocarcinomas. The last two mentioned, is the case, especially if the clinical history is not well established or if the radiologic findings are obscure, where the pathologist/cytopathologist plays a definitive role in solving the ambiguity. If the aspiration is insufficient or hypocellular owing to the nature of the lesion as it would be in an enchondroma, it would not be possible to distinguish grade I chondrosarcoma from an enchondroma cytologically, even with all the radiological data inhand. Therefore, whenever faced with a chondroid lesion which is hypocellular or with no or minimal nuclear atypia, cytopathologists should certainly refrain from defining the lesion as chondrosarcoma but still should suggest a tissue biopsy or excision of the lesion (6).

Chondrosarcomas other than grade I, are quite cellular when compared to benign chondroid lesions (2). They are most of the time suspected radiologically, by their characteristic locations and findings of the lesion (2-4). Therefore, a crucial point in cytologic diagnosis of these lesions is the cellularity (1), along with cellular atypia, macronucleoli, presence of background substance (chondroid/chondromyxoid) (1,5). Mitosis and necrosis if present, should alert the cytopathologist in favor of a high grade tumor.

In our case, the radiologic interpretation was misleading but the aspiration was quite representative of a typical chondrosarcoma, with all the cytomorphologic parameters (high cellularity, slight pleomorphism, binucleation, some degree of atypia of the nuclei) and presence of abundant chondromyxoid matrix in the background (1,3,6). The aforementioned criteria lead to the diagnosis but, mucicarmen, Pan-keratin and calretinin was applied to verify that the cells lacked the differentiation of an adenocarcinoma or mesothelioma. Pan-keratin negativity also excluded the possibility of a chordoma- although the location of the lesion and the cytomorphology of the cells were not typical of a physaliphorous cell morphology, as one would expect in chordoma (2,3). Strong cytoplasmic positivity

with vimentin and S-100 were seen and these aided in the establishment of the diagnosis. Ki-67 proliferative index has been studied in soft tissue tumors (7). In our case we also wanted to verify its significance, in a case of chondrosarcoma. Immunocytochemical application of Ki-67 to the cell block section, yielded strong nuclear positivity in 7/50 cells counted in HPF. This finding also supported the malignant potential of the lesion together with essential diagnostic criteria.

In conclusion, chondroid lesions are cytologically challenging diagnoses; and hard to grade; but whenever there are enough clues to assess, cytopathologists may very well come up with the proper diagnosis.

References

1. Lerma E, Tani E, Brosjö O, et al. Diagnosis and grading of chondrosarcomas on FNA biopsy material. Diagn Cytopathol 2003;28:13-7.
2. Inwards CY, Unni KK. Classification and grading of bone sarcomas. Hematol Oncol Clin North Am 1995;9:545-69.
3. LJ Layfield. Cytopathology of bone and soft tissue tumors. New York: Oxford University Press, 2002;178-91.
4. Wold LE, McLeod RA, Sim FH, et al. Atlas of Orthopedic Pathology. Philedelphia: WB Saunders Co., 1990;86-91
5. Jones C, Liu K, Hirschowitz S, et al. Concordance of histopathologic and cytologic grading in musculoskeletal sarcomas: can grades obtained from analysis of the fine-needle aspirates serve as the basis for therapeutic decisions? Cancer 2002;96:83-91.
6. Sanerkin NG. The diagnosis of and grading of chondrosarcoma of bone: a combined cytologic and histologic approach. Cancer 1980;45:582-94.
7. Hoos A, Stojadinovic A, Mastorides S, et al. High Ki-67 proliferative index predicts disease specific survival in patients with high-risk soft tissue sarcomas. Cancer 2001;92:869-74.