The utility of chest ultrasound-guided fine-needle biopsy in the diagnosis of plasmacytoma

S S Benbarka,[1] MD, FCP (SA), MMed (Int); **P T Shubert,**[2] MB ChB, FCPath (Anat), MMed (Anat), MSc MedSc(Cytopath), MPhil(Paed Path);
E M Irusen,[1] MB ChB, FCP (SA), PhD; **B W Allwood,**[1] MB ChB, FCP (SA), MPH, Cert Pulm (SA), PhD;
C F N Koegelenberg,[1] MB ChB, MMed (Int), FCP (SA), FRCP (UK), Cert Pulm (SA), PhD

[1] *Division of Pulmonology, Department of Medicine, Stellenbosch University and Tygerberg Academic Hospital, Cape Town, South Africa*
[2] *Division of Anatomical Pathology, Department of Pathology, Stellenbosch University and NHLS, Tygerberg Academic Hospital, Cape Town, South Africa*

***Corresponding author**: S Benbarka (ssbenbarka.bbss@gmail.com)*

Background. Plasmacytoma is a plasma cell dyscrasia originating from a single clone of plasma cells of B-lymphocyte lineage and produces a monoclonal immunoglobulin. Transthoracic fine-needle aspiration (TTNA) under ultrasound (US) guidance is a well-validated technique for the diagnosis of many neoplasms and has been shown to be safe and cost effective, with diagnostic yields comparable to more invasive techniques. However, the role of TTNA in the diagnosis of thoracic plasmacytoma is not well established.
Objective. The aim of this study was to assess the utility of TTNA and cytology in confirming a diagnosis of plasmacytoma.
Methods. All cases of plasmacytoma diagnosed from January 2006 to December 2017 by the Division of Pulmonology, Tygerberg Hospital, were retrospectively identified. All patients who underwent an US-guided TTNA and of whose clinical records could be retrieved were included in this cohort. The International Myeloma Working Group's definition of a plasmacytoma was used as the gold standard.
Results. A total of 12 cases of plasmacytoma were identified and 11 patients included (one patient was excluded owing to missing medical records). Six of the 11 patients (mean age 59.5 ± 8.5 years) were male. Radiologically, most had multiple lesions (*n*=7), most commonly bony (*n*=6) with vertebral body involvement (*n*=5) and pleural-based lesions (*n*=2). Rapid onsite evaluation (ROSE) was performed and documented in 6 of the 11 cases, and a provisional diagnosis of plasmacytoma was suggested in 5 of the 6 patients (83.3%). The final laboratory cytological diagnoses of all 11 cases were compatible with plasmacytoma which was further confirmed via a bone marrow biopsy (*n*=4) and by serum electrophoresis (*n*=7).
Conclusion. US-guided fine-needle aspiration is feasible and is useful to confirm a diagnosis of plasmacytoma. Its minimally invasive nature may be the ideal investigation of choice in suspected cases.
Keywords. Plasmacytoma, ultrasound, transthoracic fine-needle aspiration.

Afr J Thoracic Crit Care Med 2022;28(4):167-171. https://doi.org/10.7196/AJTCCM.2022.v28i4.242

Plasmacytoma is a plasma cell dyscrasia originating from a single clone of plasma cells of B-lymphocyte lineage and produces a monoclonal immunoglobulin.[1] Plasma cell neoplasms generally present as either a single lesion (solitary plasmacytoma) or multiple lesions (multiple myeloma).

A plasmacytoma can present as a solitary lesion occurring within the axial skeleton[2] or as an extramedullary plasmacytoma that occurs within soft tissue, which accounts for 5 - 10% of all types of plasma cell neoplasms.[1,3,4]

The evaluation of a patient with a suspected extramedullary plasmacytoma should include a biopsy of the suspected lesion, a bone marrow aspiration and biopsy and ancillary laboratory investigations including a full blood count, renal function, serum calcium, serum free monoclonal light chain through serum protein electrophoresis and a 24-hour urine analysis for protein electrophoresis.

Patients with plasma cell neoplasms usually have high serum protein levels.[5] Although a presumptive diagnosis is often based on a monoclonal peak on plasma electrophoresis[6,7] and the presence of urinary Bence Jones protein, a tissue diagnosis is required to make a definitive diagnosis.[5-8]

Plasmacytomas can be distinguished from most neoplasms based on the morphological appearance of the plasma cells and on their clonal nature. This can be established via immunostaining for kappa and lambda light chains or by flow cytometry. Typically, plasma cells in plasmacytoma will be positive for CD138 and CD38, and show light chain restriction (i.e. stain positive for either kappa or lambda but not both).[8]

Transthoracic fine-needle aspiration (TTNA) under ultrasound (US) guidance is a well-validated technique for the diagnosis of lung cancer and many other neoplasms, and has been shown to be safe and cost effective, with diagnostic yields comparable to more invasive techniques.[9,10] However, the role of TTNA in the diagnosis of thoracic plasmacytoma is not well established.

The aim of this study was to assess the utility of US-guided TTNA and cytology in confirming a diagnosis of plasmacytoma.

Methods

Patient population

All cases of plasmacytoma diagnosed from January 2006 to December 2017 by the Division of Pulmonology, Tygerberg Hospital, were

retrospectively identified by searching the National Health Laboratory Service (NHLS) pathology data base. All patients who underwent a US-guided TTNA during this period and of whom clinical records could be retrieved were included in a retrospective cohort. Tygerberg Hospital is a 1 380-bed, tertiary public hospital in South Africa serving approximately three million people. Ethical approval for the current study was provided by the Stellenbosch University Research Ethics Committee, protocol number (S17/02/043). The cases were reviewed for age, gender, presentation and anatomical involvement.

Transthoracic ultrasound

During the study period, a respiratory physician routinely performed the sonography with a standard 3.75-MHz sector probe. The patients' positions for scanning were determined by the corresponding computed tomography (CT) scan. All procedures were performed in a bronchoscopy suite. The intended puncture site was subsequently identified and marked, and the direction and depth of interest for the procedure documented. The site of aspiration was the epicentre of chest wall contact, and the intended direction towards the observed or anticipated location of the mass lesion while care was taken to avoid any major blood vessels or viscera. All procedures were subsequently performed 'freehand' (not under direct real-time US guidance).

Transthoracic fine-needle aspirations

Aspirations were performed with 22-G spinal needles of 40 mm or 90 mm length as needed (Tae-Cang, Kong Ju City, Korea) connected to a 10 ml syringe under sterile conditions with local anaesthesia and no sedation. Aspirates (all from slightly different directions and depths) were directly expressed onto slides, smeared and submitted for rapid onsite evaluation (ROSE) using both Diff-Quik (Rapidiff; Clinical Sciences Diagnostics, Southdale, South Africa) and rapid Papanicolaou staining methods.

Rapid onsite evaluation (ROSE) of cytology specimens

A cytopathologist was generally present at the majority of the TTNA procedures to perform ROSE of the specimens to assess their adequacy for laboratory evaluation, collect all necessary specimens (including cell blocks) and provide a preliminary diagnosis.

Data collection

The International Myeloma Working Group's definition of a plasmacytoma was used as the gold standard.[11]

Results

A total of 12 cases of plasmacytoma were identified in the present study and included 11 patients (one patient's medical records could not be retrieved). Six of the 11 patients (mean age 59.5 ± 8.5 years) were male (Table 1). The clinical presentations of the 11 patients are also summarised in Table 1. Radiologically, most of the patients had multiple lesions (*n*=7), most commonly bony (*n*=6) with vertebral body involvement (*n*=5) and pleural-based lesions (*n*=2).

ROSE was performed and documented in 6 of the 11 cases, and a provisional diagnosis of plasmacytoma was suggested in 5 of the 6 patients (83.3%). The final cytological diagnoses of all 11 cases were compatible with plasmacytoma/myeloma (*n*=11) and were further confirmed by flow cytometry (*n*=5), bone marrow biopsy (*n*=4) and serum protein electrophoresis (*n*=7). Hypercalcaemia was present in 3 cases and 2 subjects were HIV positive.

Cytological findings in a plasma cell dyscrasia (plasmacytoma) show a dis-cohesive aspirate with rather monomorphic, morphologically identifiable plasma cells, including mono- and binucleated variants (Figs 1 and 2). These cells are typically medium-sized, show little pleomorphism with round, eccentrically located nuclei with a clumped 'clock face' chromatin pattern and a perinuclear cytoplasmic clearing or hof. Small nucleoli may be seen. Some radiological findings from the patients included in this study are shown in Figs 3 - 5. These findings varied from single to multiple pleural-based masses, with or without rib destruction or vertebral body invasion. The lung appeared invaded in most cases. Fig. 6 is complementary to Fig. 4.

Discussion

In this retrospective study, we found that plasmacytoma was diagnosed in all cases through US-guided TTNA with ROSE. US-guided biopsy of the chest wall, pleural-based, and pulmonary lesions abutting the chest wall, performed by pulmonologists, is feasible and has utility. It has the advantage of multi-planar imaging, real-time technique, and the absence of radiation exposure to patients.[12,13]

Fine-needle aspiration (FNA) cytology is a well-established procedure for the diagnosis of a soft-tissue mass or any lesion in the body.[14,15] There is a paucity of high-quality data on the utility of US-guided TTNA in the diagnosis of plasmacytoma, given the fact that it remains a rare condition.[16,17] There are mainly case reports of plasmacytoma found in the pancreas, stomach, thyroid, tonsil, larynx and liver where FNA biopsy (FNAB) was successfully performed.[18,19] Endoscopic ultrasound-guided FNA has also been used in diagnosing plasmacytoma of the pancreas.[20] Gastro-intestinal plasmacytoma is rare and accounts for 10% of all plasmacytoma cases.[21]

Extramedullary plasmacytomas are very rare tumours and can be easily misdiagnosed for carcinoma (particularly well-differentiated adenocarcinoma), non-Hodgkin lymphoma and rarely for fibrous histiocytoma, rhabdomyosarcoma, dermatofibroma and sarcoma.[22,23] A definitive diagnosis needs a cellular and well-preserved cytology sample with a predominance of a relatively monomorphic, morphologically identifiable plasma cell population. These cells can include bi- and multi-nucleated forms; some pleomorphisms can be seen with larger cells and nucleoli. Not all neoplastic cells contain an abundance of cytoplasm with a perinuclear hof, and a careful search is needed. As these tumours are relatively uncommon, the cytopathologist must be aware of this possibility and a further examination for other cells needs to be undertaken to exclude other possibilities such as an inflammatory myofibroblastic tumour or IgG4 sclerosing diseases. If the plasma cells demonstrate pleomorphism or blastic nuclear features, then a plasmablastic lymphoma or diffuse large B-cell lymphoma can be considered. Plasma cells may also contain large vacuoles in their cytoplasm, mimicking a signet-ring cell carcinoma.[24,25]

FNA cytology is used to make a perioperative diagnosis as a minimally invasive procedure, especially if ROSE is made available simultaneously.[26] The accuracy of the sample is dependent on the level of experience of the team, the size of the mass, the needle size and, ideally, no blood contamination. The advantages of using ROSE for a rapid diagnosis have been demonstrated in numerous retrospective

Table 1. Clinical and investigative data of the patients (*N*=11)

Case	Age (years)	Sex	Presentation	Lesion	ROSE	Serum calcium	Serum creatinine
1	56	M	Lower-limb weakness	Multiple	Plasmacytoma	2.81	109
2	75	M	Chest mass	Single	ND	2.17	112
3	63	F	Paraspinal mass	Single	Plasmacytoma	2.46	43
4	45	M	Rib mass	Multiple	ND	2.17	69
5	52	F	Left lung tumour	Multiple	ND	3.52	73
6	62	F	Chest wall mass	Multiple	ND	2.42	63
7	52	M	Ptosis with lung mass	Multiple	Myeloma/plasmacytoma or adenocarcinoma	2.36	74
8	70	F	Pleural-based mass	Single	Adenocarcinoma*	2.50	66
9	58	M	Lower-limb weakness	Multiple	Myeloma	2.62	110
10	63	F	Pleural-based mass	Multiple	Myeloma	2.35	94
11	58	M	Right lung mass tumour	Single	ND	2.48	88

M = male; F = female; ROSE = rapid on-site evaluation; ND = not documented.
*This case was misdiagnosed as well-differentiated adenocarcinoma on-site. This is a pitfall which the cytopathologist needs to be aware of.

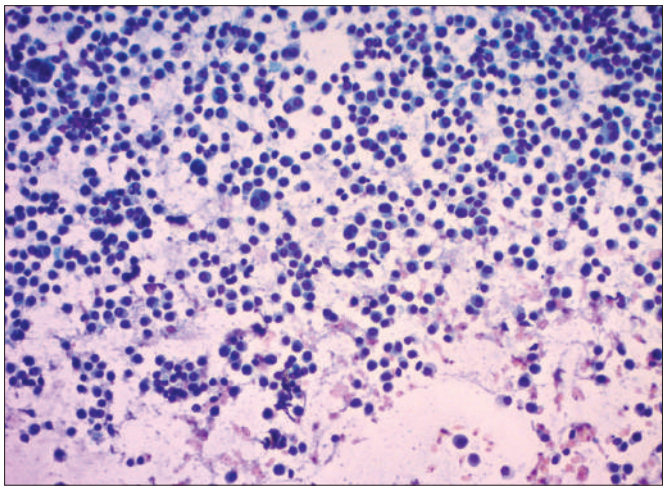

Fig. 1. Cytological findings compatible with plasmacytoma (plasma cell dyscraisa). The cells are monomorphic and medium sized, show eccentrically located nuclei with a 'clock face' chromatin pattern and a small nucleolus. Occasional bi-nucleated forms are seen (Papanicolaou stain, 400x).

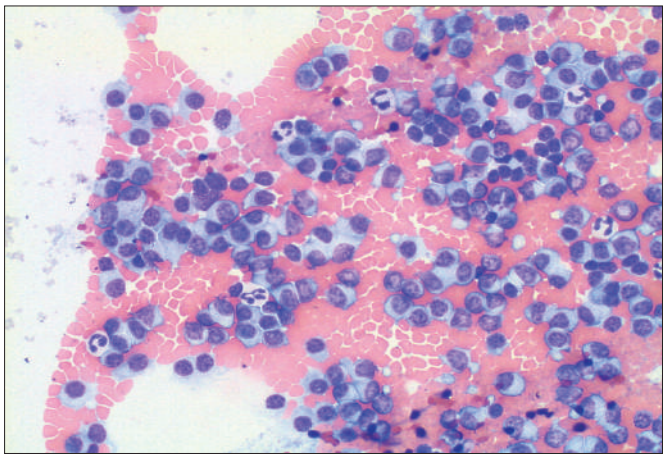

Fig. 2. Diff-Quick stained image with neoplastic plasma cells, highlighting the plasmacytoid nature of the neoplastic plasma cells (400x).

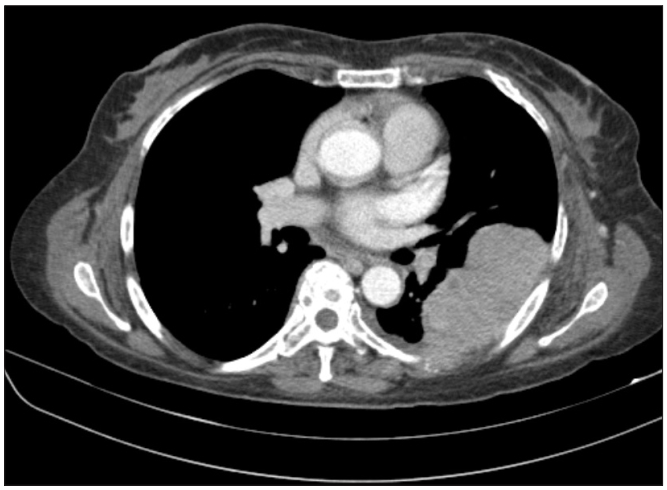

Fig. 3. A left posterior-lateral, pleural-based mass with lung infiltration, without marked rib destruction. The lesion on the computed tomography scan was reported to be suggestive of lung cancer, but ultimately proven to be a plasmacytoma.

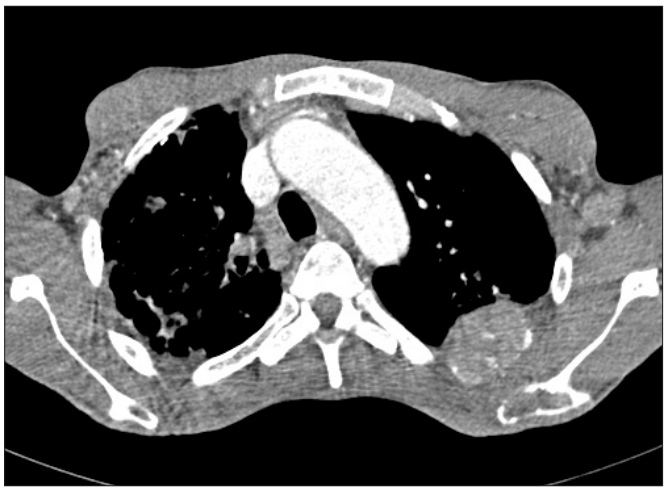

Fig. 4. Computed tomography image of a left lateral chest wall mass with marked rib destruction by a plasmacytoma and a lytic lesion of the left scapula.

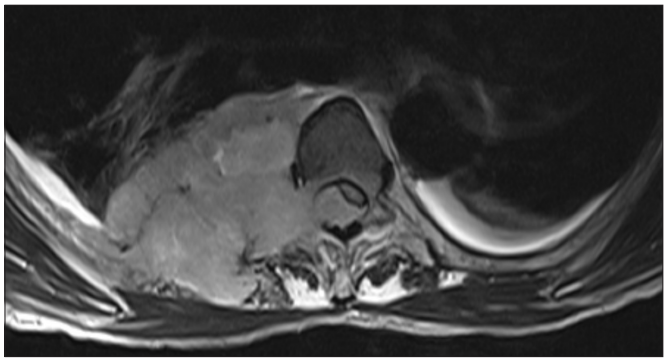

Fig. 5. A magnetic resonance image (MRI) of a patient who presented with lower-limb weakness secondary to a vertebral plasmacytoma.

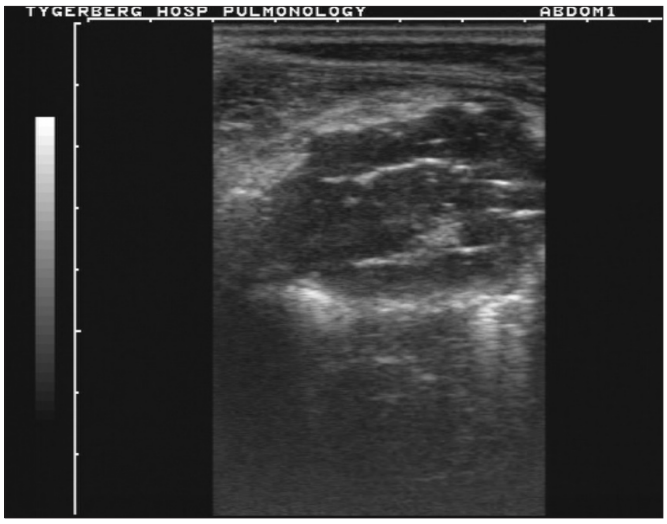

Fig. 6. Ultrasound image (high frequency) of the rib lesion seen in Fig. 4.

studies.[27-29] The impacts of using ROSE were most noticeable in the improvement of sample adequacy when performed by pathologists and at centres where initial sample adequacy rates without ROSE were low.[30]

ROSE was used in the current study and has been shown to increase the diagnostic yield in transthoracic FNAs of lung cancer as well as decreasing the procedure time. Given the small number of patients in the present study, an estimation of its full impact could not be determined.

The advantages of TTNA use under US guidance with ROSE are numerous. Benefits include an increase in the sample accuracy, improvement in sample processing quality, adequacy of the material and improvement in communication between multiple subspecialty teams, which yielded good results in the present study.

The present study also investigated the immune status of patients. There is a well-known association between plasma cell tumour and immunosuppressed patients, including HIV infection. Two patients were HIV positive in the present study, suggesting that routine testing should be recommended.

Our study has some limitations, most notably its retrospective design and that the ROSE findings were not always clearly documented. Given the incidence of plasmacytoma in the general population, only a large-scale multinational study would accurately establish the utility of ultrasound-guided FNA in the diagnosis of plasmacytoma.

In conclusion, US-guided FNA was found to be feasible and has utility in diagnosing plasmacytoma. Its minimally invasive nature may be the ideal investigation of choice in suspected cases.

Declaration. We declare that this study is our own original work and that it has not previously, neither in its entirety nor in part, been submitted to any university for degree purposes.

Acknowledgements. We thank the personnel of the Pulmonology Department at Stellenbosch University for their complete support in publishing this work.

Author contributions. This is a joint work by all listed authors.

Funding. None received.

Conflicts of interest. None.

1. Dimopoulos MA, Kiamouris C, Moulopoulos LA. Solitary plasmacytoma of bone and extramedullary plasmacytoma. Hematol Oncol Clin North Am 1999;13(6):1249-1257. https://doi.org/10.1016/S0889-8588
2. Kilciksiz S, Karakoyun-Celik O, Agaoglu FY, Haydaroglu A. A review for solitary plasmacytoma of bone and extramedullary plasmacytoma. Sci World J 2012;2012:895765. https://doi.org/10.1100/2012/895765
3. Kaur Gill M, Makkar M, Singh Bains SP. Solitary plasmacytoma of skull: A rare cytological diagnosis. J Clin Diagnostic Res 2013;7(8):1702-1703. https://doi.org/10.7860/JCDR/2013/5555.3259
4. Bush SE, Goffinet DR, Bagshaw MA. Extramedullary plasmacytoma of the head and neck. Radiology 1981;140(3):801-805. https://doi.org/10.1148/radiology.140.3.6792654
5. Haegelen C, Riffaud L, Bernard M, Carsin-Nicol B, Morandi X. Dural plasmacytoma revealing multiple myeloma. Case report. J Neurosurg 2006;104(4):608-610. https://doi.org/10.3171/jns.2006.104.4.608
6. Kubagawa H, Vogler LB, Capra JD, Conrad ME, Lawton AR, Cooper MD. Studies on the clonal origin of multiple myeloma. Use of individually specific (idiotype) antibodies to trace the oncogenic event to its earliest point of expression in B-cell differentiation. J Exp Med 1979;150(4):792-807. https://doi.org/10.1084/jem.150.4.792
7. Hughes M, Soutar R, Lucraft H, Owen R. Guidelines on the diagnosis and management of solitary plasmacytoma of bone, extramedullary plasmacytoma and multiple solitary plasmacytomas: 2009 update. UKMF Guidel Work Gr 2009:1-14. https://doi.org/10.1016/j.clon.2004.02.007
8. Weber DM. Solitary bone and extramedullary plasmacytoma. Hematology Am Soc Hematol Educ Program 2005:373-376. https://doi.org/10.1182/asheducation-2005.1.373
9. Birchard KR. Transthoracic needle biopsy. Semin Intervent Radiol 2011;28(1):87-97. https://doi.org/10.1055/s-0031-1273943
10. Koegelenberg CFN, Bolliger CT, Theron J, et al. Direct comparison of the diagnostic yield of ultrasound-assisted Abrams and Tru-Cut needle biopsies for pleural tuberculosis. Thorax 2010;65(10):857-862. https://doi.org/10.1136/thx.2009.125146
11. International Myeloma Working Group. Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders. Br J Haematol 2003;121:749-757. https://doi.org/10.1046/j.1365-2141.2003.04355.x
12. Khosla R, McLean A, Smith J. Ultrasound-guided versus computed tomography-scan guided biopsy of pleural-based lung lesions. Lung India 2016;33(5):487. https://doi.org/10.4103/0970-2113.188961
13. Corcoran JP, Tazi-Mezalek R, Maldonado F, et al. State of the art thoracic ultrasound: Intervention and therapeutics. Thorax 2017;72(9):840-849. https://doi.org/10.1136/thoraxjnl-2016-209340
14. Monaco SE. Fine needle aspiration cytology. In: McManus L, Mitchell R, editors. Pathobiology of Human Disease: A Dynamic Encyclopedia of Disease Mechanisms. Amsterdam: Elsevier, 2014; p. 3379-3398. https://doi.org/10.1016/B978-0-12-386456-7.06504-7
15. Bottles K, Miller TR, Cohen MB, Ljung B-M. Fine needle aspiration biopsy. Am J Med 2016;81(3):525-531. https://doi.org/10.1016/0002-9343(86)90309-8
16. Goel G, Rai S, Naik R, Gupta A, Baliga P, Sinha R. Cytodiagnosis of extramedullary plasmacytomas. Acta Cytol 2010;54(3):255-258. https://doi.org/10.1159/000325031
17. Kumar PV, Owji SM, Talei AR, Malekhusseini SA. Extramedullary plasmacytoma. Fine needle aspiration findings. Acta Cytol 1997;41(2):364-368.
18. Roh YH, Hwang SY, Lee SM, et al. Extramedullary plasmacytoma of the pancreas diagnosed using endoscopic ultrasonography-guided fine needle aspiration. Clin Endosc 2014;47(1):115-118. https://doi.org/10.5946/ce.2014.47.1.115
19. Husney J, Guttmann S, Anyadike N, Mayer I, Rahmani R. Endoscopic ultrasound-fine needle aspiration: A novel way to diagnose a solitary extramedullary plasmacytoma of the liver. Endosc Ultrasound 2016;5(2):134-136. https://doi.org/10.4103/2303-9027.180481

20. Williet N, Kassir R, Cuilleron M, et al. Difficult endoscopic diagnosis of a pancreatic plasmacytoma: Case report and review of literature. World J Clin Oncol 2017;10(81):91-95. https://doi.org/10.5306/wjco.v8.i1.91
21. Ames J, Al-Samaraee A, Takahashi T. Extraosseous multiple myeloma: Case report of presentation in the lower extremity soft tissues with literature review. Case Rep Radiol 2017;2017:1-9. https://doi.org/10.1155/2017/9159035
22. Morris RW, Kumar V, Saad AG. Anaplastic plasmacytoma: A rare tumor presenting as a pathological fracture in a younger adult. Skeletal Radiol 2018;47(7):995-1001. https://doi.org/10.1007/s00256-018-2884-x
23. Santiago FR, Moreno MT, Castro AM, Álvarez LG, González PN. Soft tissue extramedullary plasmacytoma. Case Rep Med 2010;2010:10-13. https://doi.org/10.1155/2010/307902
24. Handa U, Bal A, Mohan H, Bhardwaj S. Fine needle aspiration cytology in the diagnosis of bone lesions. Cytopathology 2005;16(2):59-64. https://doi.org/10.1111/j.1365-2303.2004.00200.x
25. Field AS, Geddie WR. Lymph node and spleen cytohistology. New York: Cambridge University Press; 2014.
26. Bhat R, Prathima K, Harendra Kumar M, Narayana G. Plasmacytoma of tonsil diagnosed by fine-needle aspiration cytology. J Cytol 2010;27(3):102. https://doi.org/10.4103/0970-9371.71875
27. Schmidt RL, Witt BL, Lopez-Calderon LE, Layfield LJ. The influence of rapid onsite evaluation on the adequacy rate of fine-needle aspiration cytology: A systematic review and meta-analysis. Am J Clin Pathol 2013;139(3):300-308. https://doi.org/10.1309/AJCPEGZMJKC42VUP
28. Brundyn K, Koegelenberg CFN, Diacon AH, et al. Transbronchial fine needle aspiration biopsy and rapid on-site evaluation in the setting of superior vena cava syndrome. Diagn Cytopathol 2013;41(4):324-329. https://doi.org/10.1002/dc.21857
29. Koegelenberg CFN, Bolliger CT, Plekker D, et al. Diagnostic yield and safety of ultrasound-assisted biopsies in superior vena cava syndrome. Eur Respir J 2009;33(6):1389-1395. https://doi.org/10.1183/09031936.00128108
30. Eisendrath P, Ibrahim M. How good is fine needle aspiration? What results should you expect? Endosc Ultrasound 2014;3(1):3-11. https://doi.org/10.4103/2303-9027.127122

Accepted 27 September 2022.