Introduction

Primary tumors develop rarely in the spine, but metastases are more frequently evidenced [1]. Data suggest that the spine is the most common site for metastases and for lesions of unknown origin [1,2]. Vertebral primary tumors or metastases represent a difficult target for percutaneous ultrasound (US) guided biopsies, being performed usually under computed tomography (CT) guidance [3]. Osteolytic benign tumors are more frequent in the pediatric population [4]. In rare cases, non-ossifying fibromas and fibrous histiocytomas can be located also in the vertebrae [5-7]. Also, aneurysmal bone cysts can be found in the vertebrae, both in adult and in pediatric populations [8,9]. Frequently, histopathological examination of the suspected lesions establishes the final diagnosis; therefore, procurement of the tissue is of the utmost importance [10]. Although bone tumors are rare, histopathological examination is often difficult [10]. Some authors and expert groups have even defined the “ideal lesions”, potential lesions and also the contraindications...
for bone biopsies [10]. Among these “ideal lesions” are: carcinoma and melanoma metastases, monomorphic tumoral proliferations, Ewing or Ewing-like sarcoma, lymphoma, plasmocytoma [10]. Surgical biopsies are associated with higher complication rates than image-guided approaches; therefore, whenever possible, the minimally invasive diagnosis technique has to be envisaged [11,12]. Also, there are numerous cases when the path to the final diagnosis is long and difficult, such as for lung cancer, when histological diagnosis can be even more challenging if the tumor cannot be biopsied by the transbronchial route and transesophageal ultrasound (EBUS) or endoscopic ultrasound (EUS) fine needle aspiration (FNA). In those cases, if the ventilated lung should be passed along the biopsy tract, the CT-guided biopsy entails a higher number of complications [13,14].

To our knowledge, there are only two published case reports of EBUS guided vertebral metastasis – one using a transtracheal, the other using a transesophageal approach with echobronchoscopes – but none using a transesophageal dedicated echoendoscope [15,16]. Therefore, our aim is to present an alternative for the “classical approach” – the conventional open surgical biopsies or CT guided biopsies. We present our series of four cases diagnosed by trans-esophageal and trans-gastric EUS FNA of the vertebral body osteolytic tumors and metastases of various origins.

**Cases presentations**

**Case 1**

A 62-year-old man was referred for a lung biopsy from a right upper lobe lung tumor (fig 1a) with osteolytic metastasis located at the lower cervical and dorsal vertebral bodies (fig 1b) revealed by thoracic CT. The patient complained of dorsal pain, associated with left abdominal upper quadrant pain, with progressive evolution, which had appeared 3 months prior to admission. He was smoker (30 pack-years) and hypertensive. The bronchoscopy did not visualize the tumor. Transthoracic US could not evidence the tumor due to the interposition of the ventilated lung between the pleura and the tumor. Analyzing the thoracic CT scan, we considered that a transesophageal EUS-FNA biopsy of the dorsal vertebral body metastasis could be feasible. Transesophageal EUS examination under propofol deep sedation was performed, using a linear Olympus® echoendoscope GF UCT180, showing a gastric ulcer, chronic erosive gastritis and multiple mediastinal lymph nodes with suspicious features, associated with two hypoechoic osteolytic protruding masses originating from two vertebral bodies (fig 1c). EUS guided FNA was realized in the same session – 3 passages with a 22G Olympus EZ Shot® 3 Plus (Tokyo, Japan) needle – using dry suction - procuring cylindrical tissue specimens (fig 1d). Histopathological and immunohistochemical examination revealed the esophageal wall structure and a malignant tissue with features of metastatic adenocarcinoma, with glandular arrangements of the malignant cells, CK7 positive and TTF-1 negative. The patient was sent thereafter to the oncology department with T3N3M1 stage lung adenocarcinoma and chemotherapy was initiated.

**Case 2**

A 66-year-old man, active tobacco (20 pack-years) and ethanol consumer, presented for dorsal, lumbar and left thigh pain with left intercostal irradiation, symptoms which had appeared 2 months prior to the presentation in our Department. The CT scan rised the possibility of a pancreatic tumor and showed multiple hepatic and bone metastases. Bone metastases were located in L1 vertebral pedicle and transverse process (fig 2a). EUS examination was performed under propofol deep sedation, with a

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**Fig 1.** Lung cancer with osteolytic metastases of a dorsal vertebral body: a) Thoracic axial CT scan (lung window) – showing the posterior upper right lobe lung tumor with malignant features, without a sufficient pleural contact in order to be visualized and punctured under percutaneous US-guidance; b) Thoracic axial CT scan – showing an osteolytic lesion of a dorsal vertebral body (large arrow), in proximity with the esophagus (small arrow); c) Transesophageal EUS with linear transducer showing a large hypoechoic mass posterior to the esophagus, vascularized in Color Doppler mode, representing an osteolytic metastasis of a vertebral body with extensive anterior periosseous growth; d) EUS FNA of the vertebral osteolytic lesions, with the hyperechoic needle visible inside the hypoechoic tumor (arrow).
linear Olympus® echoendoscope GF UCT180 and characterized the L1 vertebral metastasis and liver metastasis (fig 2b). EUS guided FNA of the L1 vertebral body was performed – 2 passages with a 22G Olympus EZ Shot® 3 Plus needle (Tokyo, Japan) (fig 2c), using dry suction and procured tissue specimens. EUS-FNA of one the hepatic metastasis from the left lobe and of the body pancreatic lesion was also performed. Histopathological and immunohistochemical examination of all biopsies were diagnostic. Final diagnosis from all biopsied sites was pancreatic adenocarcinoma (fig 2d). The patient was referred to the Oncology Department with metastatic pancreatic adenocarcinoma and chemotherapy was initiated.

**Case 3**

A 47-year-old man was referred for dorsal and lumbar pain irradiating to the thigh, associated with paraparesis, paresthesia and numbness, symptoms which had appeared 3 months prior to the presentation in our Department. MRI examination revealed bone metastasis located on the D10 and D11 vertebrae, extending in the dural space (fig 3a). Lymphoma or myeloma were suspected, therefore an osteomedullary biopsy (iliac bone) was performed, but the histopathological report did not confirm the diagnosis. The US examination revealed an osteolytic mass located vertebrally and paravertebrally, with extension to the posterior thoracic wall, mainly on the left side. Thoracic CT scan confirmed the presence of the osteolytic lesion (fig 3b). EUS was performed under propofol deep sedation, with a linear Olympus® echoendoscope GF UCT180 and a mediastinal paravertebral tumor was visualized. Also, the fracture of the anterior surface of the vertebral body was described (fig 3c) and another hypoechoic nodule located paraesophageally was depicted. FNA was performed both from the paraoesophageal lesions and from the paravertebral lesion (fig 3d). Histopathological and immunohistochemical examination of the paravertebral lesion specimen reported a diffuse large B cell lymphoma (LCA positive, with CD20 positive, CD23 and CD10 negative lymphocytes). The patient was referred to the Hematology Department with vertebral B cell lymphoma and chemotherapy was started.

**Case 4**

A 60-year-old male patient, with type 2 diabetes, chronic hepatitis B and atrial fibrillation, was referred for supplementary investigation of a subhepatic tumor with hepatic metastases and metastatic subhepatic lymph nodes. MRI imaging confirmed the tumor invading the duodenal wall and the head of the pancreas, with he-
Fig 4. Hepatocarcinoma with D1 vertebral body metastases. a) Axial CT scan showing an osteolytic lesion at D1 vertebral body (arrow), protruding anteriorly as a hypodense tumor; b) Transesophageal EUS revealed a hypoechogenic tumor with hypoechoic foci (vertebral bone fragments) situated posterior to the superior esophagus; EUS FNA of the D1 vertebral metastases with the image of the 22G needle inside the tumor; c) Hep-Par positive cytoplasmic granular cells confirming vertebral metastases from hepatocarcinoma (40x).

Discussion

This case series shows that EUS FNA, a minimal invasive diagnosis procedure, is a feasible alternative for selected patients. We present this diagnostic approach for osteolytic lesions of the vertebrae using transesophageal and transgastric EUS FNA biopsy of the bone lesions with lower risks for selected lesions. Though CT guided biopsies is the technique currently used, this case series brings to light that there is also another viable alternative procedure suitable for osteolytic lesions with certain features.

Suspicion of advanced neoplasia raises some key questions in the diagnostic algorithm: how can we confirm the cancer offering less complications and discomfort for the patients? In our cases, the “classical” method for targeting the primary tumor would have been the CT guided transthoracic biopsy but with possible complications, some of them potentially severe. In addition to the irradiation both for the patient and the medical staff, an open surgical biopsy results in greater risks and complications. On the other hand, a transesophageal EUS guided biopsy of the vertebral bodies with osteolytic metastasis could produce fewer and less severe complications, besides resulting in considerably less discomfort. These advantages are due to deep sedation and smaller needle calibers, which avoid the passage of the ventilated lung and subsequently lowers associated risks in comparison with other diagnostic modalities. Percutaneous US-guided biopsy of osteolytic lesions provides a good diagnostic yield with a low rate of complications and with a relatively small number of needle passages [17]. Also, having a good experience in mediastinal ultrasonography [18] and EUS FNA of the lung tumors [19], we chose to perform EUS FNA of the osteolytic vertebral lesions, a new type of EUS guided biopsy. Rapid on-site examination was not available at that moment and samples were sent to the Pathology Department. We used the same type of needle in all cases and for all biopsy sites the 22G Olympus EZ Shot® 3 Plus needle.

In the first case, immunohistochemistry applied to the biopsy specimen revealed CK-7 positive tumor cells, accompanied by TTF-1 negative nuclei. It is known that at least 12.8% of lung adenocarcinoma are TTF-1 negative and are correlated with an unfavorable prognosis [20]. The second case supports the possibility of expanding the range of vertebral body biopsies to the lumbar spine – at least until L1 level. The third case also supports the value of the EUS-FNA even with 22G needle caliber for the diagnosis of a vertebral B cell lymphoma. The fourth case represents a premiere for us, as we diagnosed by EUS a previously unknown dorsal vertebral body (D1) osteolyt-
ic metastasis and confirmed the finding with a subsequent thoracic CT scan.

In the cases with multiple sites sampling, the pathological analysis revealed the same malignant disease in all sites – pancreatic adenocarcinoma in case no. 2 and hepatocarcinoma in case no. 4.

Frequently, in lymphomas, bone or lymph node biopsies establish the diagnosis, but in our case the diagnosis was established by the biopsy of a vertebral body osteolytic lesion. EUS-FNA could be also useful in the cases of extra medullary hematopoesis, when the liver or/and the spleen could be biopsied even during the same examination [21,22].

We found only two case reports published, both of them using endobronchial echoendoscopes (EBUS), one using a transtracheal and the other a transesophageal approach for procuring samples of dorsal vertebral bodies [15,16].

Despite the small number of cases in our series – 4, this is the first report of the EUS-FNA use in osteolytic lesions, and all cases provided enough material in order to establish the final histopathological diagnosis. The advantages of this technique are undoubtedly the premises for including the procedure in the armamentarium of spine tumors investigations, and possibly in the guidelines.

Beside the advantages of this diagnostic technique, we hope that with this approach it would be interesting and challenging to use also EUS-guided radio frequency ablation (RFA) of vertebral osteolytic lesions. For some bone tumors - osteoid osteoma for example - RFA is now the standard of care [3,23]. Beside the ability to be a curative therapy for certain benign lesions, RFA is also used as palliative therapy in patients with bone metastasis [3,24,25]. An example is the anterior lesions of the vertebral body, where a percutaneous biopsy or percutaneous RFA is difficult to be performed.

Our case series also illustrates the range of potential indications of EUS FNA for vertebral body biopsy: from dorsal to first lumbar vertebrae. Judging according to our clinical practice, also the inferior cervical vertebrae can be accessible for this procedure. This range is probably dependent also on the individual characteristics of the patient. This approach could represent an option in selected cases, when percutaneous biopsies are not possible, or when surgical risks are major or the patient prefers a non-invasive alternative less risky and more cost-efficient.

Therefore, to our knowledge, our cases are the first reported use of an endoscopic ultrasound device designed for transesophageal examination for a biopsy of a dorsal and lombar vertebral osteolytic lesion, providing the final histopathological diagnosis in all four cases.

**Conclusions**

We present the first case series of a novel approach for the biopsy of osteolytic vertebral tumors – transesophageal EUS FNA. In all our four cases the EUS guided biopsy provided enough material for an adequate histopathological assessment which led to the final diagnosis. EUS FNA can provide a less invasive and efficient minimally invasive diagnostic approach to vertebral body osteolytic lesions, which until now has not been considered. However, it is a feasible, low-risk procedure.

**Conflict of interest:** none

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**References**

1. Piccioli A, Maccauro G, Spinelli MS, Biagini R, Rossi B. Bone metastases of unknown origin: epidemiology and principles of management. J Orthop Traumatol 2015;16:81-86.
2. Ugras N, Yalcinkaya U, Akesen B, Kanat O. Solitary bone metastases of unknown origin. Acta Orthop Belg 2014;80:139-143.
3. Hillen TJ, Baker JC, Jennings JW, Wessell DE. Image-guided biopsy and treatment of musculoskeletal tumors. Semin Musculoskelet Radiol 2013;17:189-202.
4. Tan E, T Mehlman C, Baker M. Benign Osteolytic Lesions in Children With Previously Normal Radiographs. J Pediatr Orthop 2017;37:e282-e285.
5. Destouet JM, Kyriakos M, Gilula LA. Fibrous histiocytoma (fibroxanthoma) of a cervical vertebra. A report with a review of the literature. Skeletal Radiol 1980;5:241-246.
6. Grohs JG, Nicolakis M, Kainberger F, Lang S, Kotz R. Benign fibrous histiocytoma of bone: a report of ten cases and review of literature. Wien Klin Wochenschr 2002;114:56-63.
7. Pere P, Adolphe J, Raul P, Delgoiffe C, Gaucher A. Nonossifying fibroma with vertebral localization. Rev Rhum Mal Osteoartic 1984;51:58.
8. Zileli M, Isik HS, Ogut FE, Is M, Cagli S, Calii C. Aneurysmal bone cysts of the spine. Eur Spine J 2013;22:593-601.
9. Hauschild O, Ludemann M, Engelhardt M, et al. Aneurysmal bone cyst (ABC) : treatment options and proposal of a follow-up regime. Acta Orthop Belg 2016;82:474-483.
10. Galant C, Bouvier C, Larrousse F, et al. Histological diagnosis of bone tumors: Guidelines of the French committee of bone pathologists reference network on bone tumors (RESOS). Bull Cancer 2018;105:368-374.
11. Ceraulo A, Ouziel A, Lavergne E, et al. Percutaneous guided biopsy for diagnosing suspected primary malignant bone
tumors in pediatric patients: a safe, accurate, and cost-saving procedure. Pediatr Radiol 2017;47:235-244.
12. Traina F, Errani C, Toscano A, et al. Current concepts in the biopsy of musculoskeletal tumors. J Bone Joint Surg Am 2015;97:e7.
13. Heerink WJ, de Bock GH, de Jonge GI, Groen HJ, Vliegenthart R, Oudkerk M. Complication rates of CT-guided transthoracic lung biopsy: meta-analysis. Eur Radiol 2017;27:138-148.
14. Yan W, Guo X, Zhang J, et al. Lobar location of lesions in computed tomography-guided lung biopsy is correlated with major pneumothorax: A STROBE-compliant retrospective study with 1452 cases. Medicine (Baltimore) 2019;98:e16224.
15. Ojha S, Le S, Boyd M, Rubio E. Vertebral body tumor biopsy: An expanded role of endobronchial ultrasound-guided transbronchial needle aspiration. J Bronchology Interv Pulmonol 2014;21:85-87.
16. Oki M, Saka H, Ichihara S, Moritani S. Transesophageal Bronchoscopic Ultrasound-Guided Fine-Needle Aspiration for Metastatic Vertebral Body Lesion. J Bronchology Interv Pulmonol 2017;24:156-158.
17. Chira RI, Chira A, Manzat-Saplacan RM, et al. Ultrasound-guided bone lesions biopsies - a systematic review. Med Ultrason 2017;19:302-309.
18. Chira RI, Chira A, Mircea PA, Valean S. Mediastinal masses-transthoracic ultrasonography aspects. Medicine (Baltimore) 2017;96:e9082.
19. Chira RI, Chira A, Ichim VA, et al. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) of paraesophageal lung tumors - diagnostic yield and added value. Med Ultrason 2019;21:377-381.
20. Zhang Y, Wang R, Li Y, et al. Negative Thyroid Transcription Factor 1 Expression Defines an Unfavorable Subgroup of Lung Adenocarcinomas. J Thorac Oncol 2015;10:1444-1450.
21. Jenssen C, Moller K, Wagner S, Sarbia M. Endoscopic ultrasound-guided biopsy: diagnostic yield, pitfalls, quality management. Z Gastroenterol 2008;46:897-908.
22. Saab S, Challita Y, Holloman D, Hathaway K, Kahaleh M, Nieto J. Case Series Review of the Safety and Efficacy of Endoscopic Ultrasound-Guided Splenic Mass Core Biopsy. Clin Endosc 2018;51:600-601.
23. Rosenthal D, Callstrom MR. Critical review and state of the art in interventional oncology: benign and metastatic disease involving bone. Radiology 2012;262:765-780.
24. Dupuy DE, Liu D, Hartfeil D, et al. Percutaneous radiofrequency ablation of painful osseous metastases: a multicenter American College of Radiology Imaging Network trial. Cancer 2010;116:989-997.
25. Callstrom MR, Charboneau JW, Goetz MP, et al. Image-guided ablation of painful metastatic bone tumors: a new and effective approach to a difficult problem. Skeletal Radiol 2006;35:1-15.