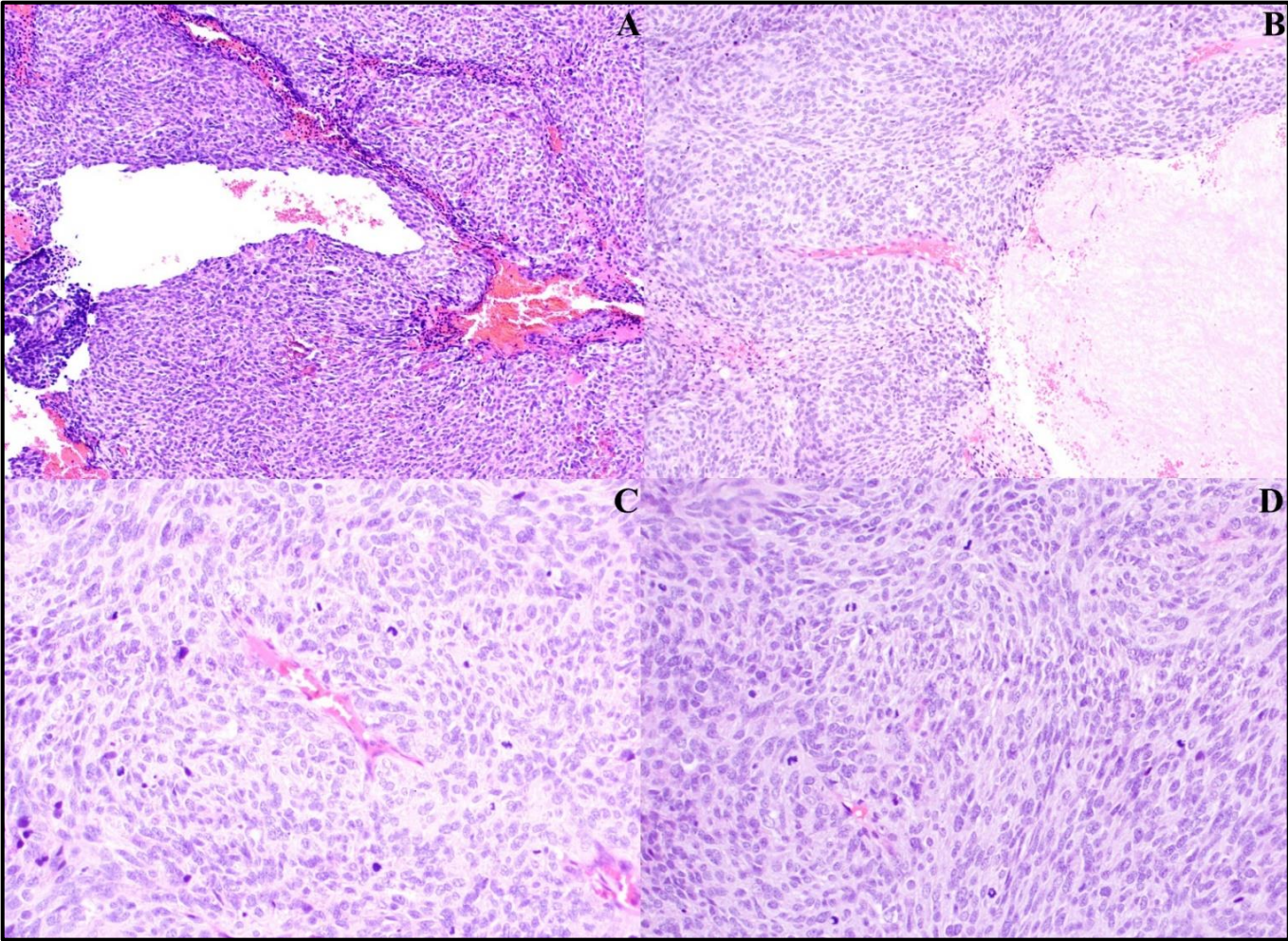


An undifferentiated sarcoma of bone with a round to epithelioid cell phenotype harboring a novel EWSR1-SSX2 fusion identified by RNA-based next-generation sequencing

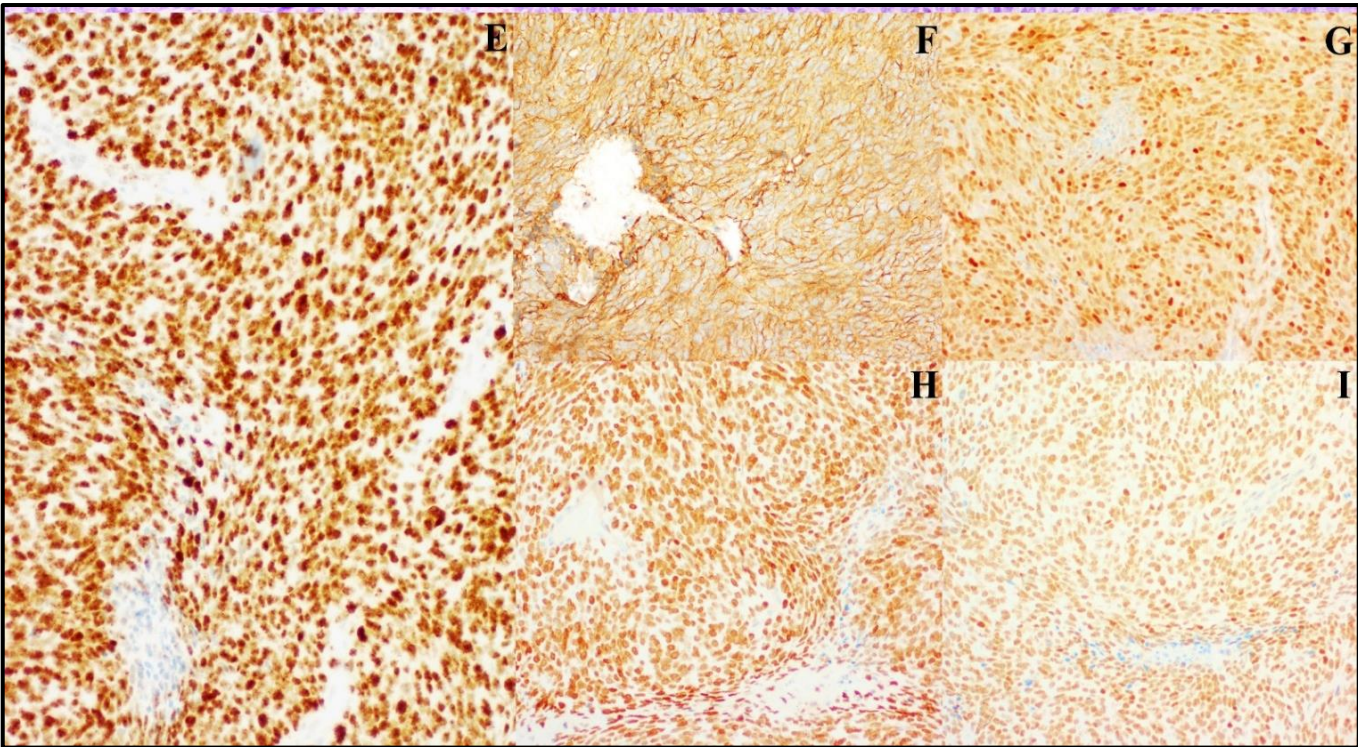
Introduction

Due to the increased application of RNA-based next-generation sequencing techniques on bone and soft tissue round cell sarcomas new fusions are frequently found, leading to the introduction of new sarcoma entities such as *CIC*-rearranged sarcomas, sarcomas with *BCOR* genetic alterations and round cell sarcomas with *EWSR1*-non-ETS (in particular *NFATC2* and *PATZ1*) fusions. These entities are now incorporated in the recent 2020 5th edition World Health Organization (WHO) Classification. Despite the significant advancement in the molecular classification of small round cell sarcomas of bone and soft tissue, pathologists are still facing cases with an undifferentiated phenotype that do not fit within the current WHO classification and remain ‘unclassified’. In this case report we describe the finding of an undifferentiated sarcoma of the bone with a round to epithelioid cell phenotype harboring a novel EWSR1-SSX2 fusion.

Case

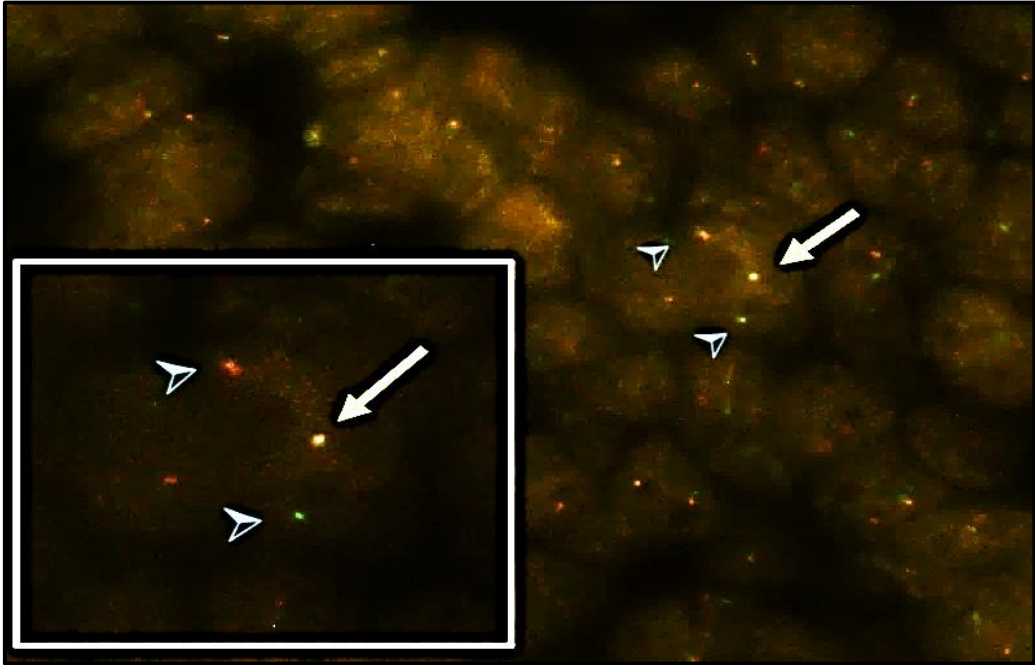


- Cellular, undifferentiated tumor.
- Round to epithelioid cells arranged in solid sheets mixed with solid areas of more spindle tumor cells showing more pleomorphism.
- Brisk mitotic activity, apoptosis and marked tumor necrosis.
- ‘Ectatic’ vessels in the background.

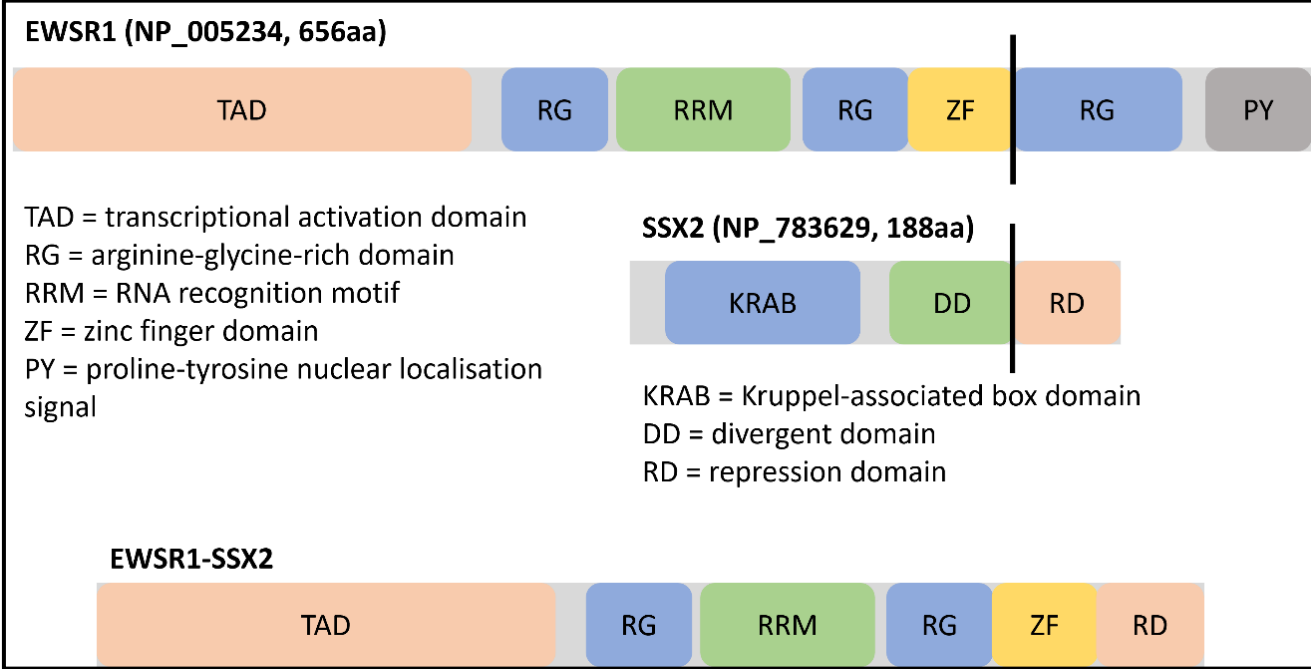


- Positivity for BCOR (E), CD99 (F), Cyclin D1 (G), SATB2 (H) and TLE1 (I).

FISH: EWSR1 rearrangement



RNA-based next-generation sequencing



Discussion and Conclusion

- EWSR1-SSX2 fusion has not yet been described in the literature.
- It could be a new member belonging to the heterogeneous group of round cell sarcomas with EWSR1-non-ETS fusion.
- Recently Antonescu et al. described 2 cases of poorly differentiated sarcomas with round cell to epithelioid morphology, both harboring a novel EWSR1-SSX1 fusion.
- Our patient was treated according to the Euro Ewing 2012 protocol with a complete histological tumor response.
- Confirmation by additional cases of undifferentiated sarcomas with EWSR1-SSX2 fusions are necessary to unravel the underlying molecular mechanisms guiding this novel EWSR1-SSX2 fusion and to better characterize their place in the evolving classification of fusion-positive undifferentiated round cell sarcomas.