Case 6
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Case history: A 21 year-old man presented with a pelvic tumor in December 1998. MRI showed a 12 cm tumor with involvement of iliac bone and muscles. A surgical biopsy was performed.

Histological and biological description:
The tumor is composed of small round and oval cells arranged in sheets with some whorling. Cells showed a monotonous nuclear with about 10 mitoses per 10 HPF. There was no necrosis on the sample. Immunohistochemistry showed a positivity for CD99 whereas pankeratin AE2/AE3, EMA, S100 protein, CD34, desmin and smooth muscle actin were negative.

RT-PCR performed on RNA extracted from frozen tissue showed no transcript for Ewing sarcoma (FLI1, ERG) and synovial sarcoma (SSX1, SSX2 and SSX4). At this moment, the final diagnosis was Undifferentiated small cell sarcoma.
The patient received a neoadjuvant chemotherapy and a surgical resection of the tumor was performed followed by a local radiotherapy and an adjuvant chemotherapy.

A local recurrence occurred in March 2004 and the patient died in May 2006.

A subsequent research program initiated in 2011 by Olivier Delattre team (Institut Curie, Paris) described a new translocation in a subset of small cell sarcomas with a \( BCOR \)-\( CCNB3 \) gene fusion. This case showed this specific translocation.

Final diagnosis: Small cell sarcoma with a \( BCOR \)-\( CCNB3 \) gene fusion.

Discussion:
Technique of RNA-seq with paired-end sequencing on a SOLiD platform was performed on 4 cases of undifferentiated small cell sarcomas with no known transcript (2). This strategy allowed to identify a new fusion gene inside chromosome X linking \( BCOR \) and \( CCNB3 \) genes on one case. This result was confirmed by RT-
PCR. Screening of 594 small cell sarcomas with no known transcripts identified a total of 24 cases with this new fusion gene.

Two-third of patients were male aged from 6 to 26 years. 19 occurred in bone and 5 in soft tissue. Follow-up was known in 16 patients with 4 with metastasis, 7 with local recurrence and 7 who died. Histologically, tumors were composed of small round or short spindle monotonous cells arranged in sheets or in whorls. Immunohistochemistry showed a CD99 positivity in 17 cases and a CD56 positivity in 18 cases. Pankeratin, EMA, CD34, SMA, desmin and chromogranin were negative. S100 protein was focally positive in 3 cases.

This new tumor showed an overexpression of BCOR and immunohistochemistry showed a diffuse nuclear positivity. Diagnosis could be confirmed by FISH or RT-PCR.

Expression profiling showed that this tumor is different from Ewing sarcoma and other round cell tumors.

The new version of WHO classification of tumours of soft tissue and bone introduced a chapter on Undifferentiated sarcomas. These tumors will be separated into 2 categories: undifferentiated pleomorphic sarcomas usually showing a complex genomic profile with no specific genomic abnormalities, and undifferentiated round cell and spindle cell sarcomas usually composed of monotonous cells. A specific genomic abnormality should always be looked for the known specific fusion genes, such as for Ewing sarcoma and synovial sarcoma, but also for new still unknown fusion genes such as BCOR-CCNB3 one. In this category of undifferentiated sarcomas, another specific gene has been reported and seems to be quite frequent in the category of Ewing sarcoma with no transcript (1).

The new technique of genome wide screening for gene fusion by RNA (exon) sequencing is a powerful technique for detecting this new fusion genes. Recently, Wang et al (3) described a specific fusion gene using a genome-wide bioinformatic screen for gene fusions with Affymetrix Exon array expression data.

References