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First Experience of NTRK Sarcoma in Lithuania: from Challenging Diagnosis to Targeted Therapy

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Introduction: Neurotrophic tyrosine receptor kinase (NTRK) gene fusions are drivers initiating oncogenic pathways in various tumors. Tropomyosin-related kinase (TRK) inhibitors are highly selective for the TRK family receptors. After the discovery of NTRK gene fusions, the treatment has become more personalized and effective by usage of targeted therapy. One of the orally administered drugs, which shows a promising efficacy in LMNA-NTRK1 soft-tissue sarcomas is Larotrectinib.

Case description: A 9-year-old girl presented with a distinct mass on her left thigh, posteriorly above popliteal region and 5-6 kg loss of weight within 6 months. Patient also complained of the pain in her left thigh, more intense at night, and dry cough. Instrumental examination showed locally advanced large tumor (69x54x115mm) of the thigh without signs of overgrowth into the femur, but with multiple metastasis in both thighs and calves, and multiple pulmonary metastases with pleural involvement. Performed biopsy indicated a low-grade infantile fibrosarcoma-like neoplasm, which was specified to be LMNA-NTRK1 subtype. Complete surgical resection was not possible, however surgery of a metastatic mass from the left thigh was performed due to patient's complaints of pain. Within one month after the diagnosis, no signs of tumour progression was observed on whole body MRI, thus patient was administered oral tyrosine receptor kinase (TRK) inhibitor Larotrectinib 100 mg twice daily. Within 3 months TRK inhibitor led to a remarkable response: disappearance of dry cough, significant decrease of primary tumour and near-complete resolution of metastases in both legs and lungs. At 12 months of targeted therapy, the patient retains response (stable disease) and favorable safety.

Conclusions: This report describes a first type of NTRK-rearranged paediatric soft tissue sarcoma in Lithuania. Testing for NTRK gene fusions in paediatric tumours with nonspecific morphology is highly important because of the recent availability of targeted therapy. The efficacy of Larotrectinib has been demonstrated to be rapid and durable with various tumour types, including soft-tissue sarcomas. Our experience treating the patient with Larotrectinib showed a positive response with minimal toxicity. Personalized therapy allows controlling the disease, when conventional treatment could not be applied.