Eur J Dermatol 2018 (epub ahead of print)

CORRESOPONDENCE

# Primary cutaneous Ewing sarcoma in a young girl

A seven-year-old girl presented with a non-progressive erythematous nodule of 5 mm in diameter that had appeared on the back of her right hand one year earlier (*figure 1A*). Excision of the tumour by shave-coagulation was conducted. Histopathological analysis revealed a circumscribed lesion in the reticular dermis composed of densely packed sheets of small and uniform cells with a pseudovascular pattern (*figure 1B, C*). Immunohistochemical analysis demonstrated a strong positive CD99 cell membrane signal, suggestive, but not specific to, cutaneous Ewing sarcoma

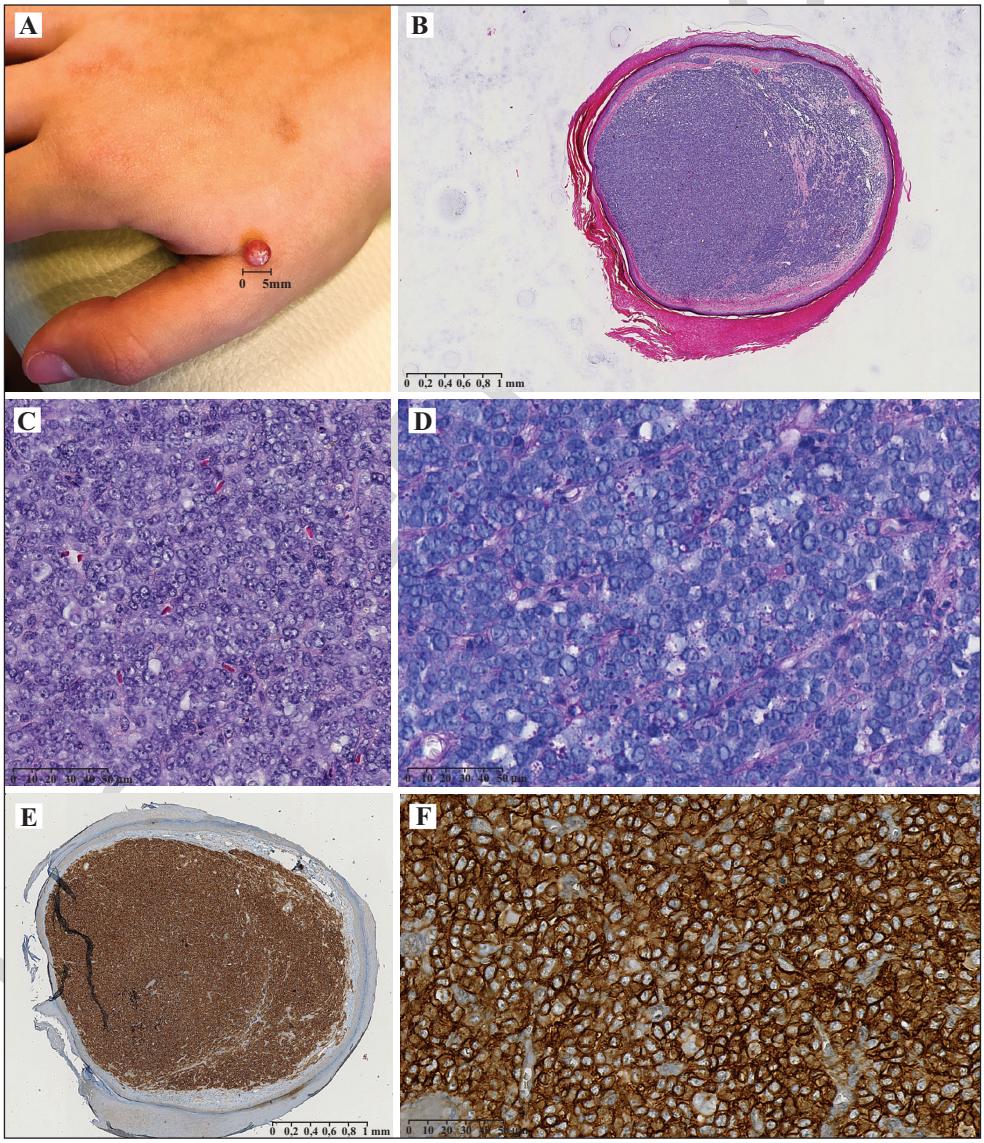


**Figure 1.** Clinical and histopathological features. **A**) Nodular erythematous lesion on the back of the right hand, between the first and second metacarpal. **B**) Nodular lesion in the derma (haematoxylin-eosin stain; x2.5 magnification). **C**) Densely packed sheets of small uniform cells (haematoxylin-eosin stain; x40 magnification). **D**) Cytoplasmic granular PAS positivity of tumour cells (Periodic acid-Schiff stain; x48 magnification). **E**) CD99 expression in tumour cells. **F**) Strong positive CD99 cell membrane signal.

doi:10.1684/ejd.2018.3477



To cite this article: Dekeuleneer V, El Nemnom P, Vervier J, Brichard B, Libert J, Van Eeckhout P, Marot L, Tennstedt D, Levy G, De Ville De Goyet M, Boulanger C. Primary cutaneous Ewing sarcoma in a young girl. *Eur J Dermatol* 2018 (epub ahead of print) doi:10.1684/ejd.2018.3477

(*figure 1E, F*). Tumour cells also stained positive for cytoplasmic granular PAS (periodic acid-Schiff) (*figure 1D*).
Molecular analysis using fluorescence *in situ* hybridisation (FISH) confirmed the diagnosis of Ewing sarcoma (ES) by revealing a specific chromosomal translocation involving the *EWSR1* (Ewing sarcoma breakpoint region 1) gene on chromosome 22 and *FLI1* (Friend leukaemia virus integration 1) gene on chromosome 11, leading to an oncogenic fusion.
The extended workup, including radiography and echography of the right hand, as well as magnetic resonance imaging and positron emission computed tomography, proved negative.
The final diagnosis was primary cutaneous Ewing sarcoma (pCES).
Although the lesion was restricted to the skin and well-defined, the patient's young age and the tumour's metastatic potential prompted us to initiate neoadjuvant chemotherapy, followed by surgery and maintenance chemotherapy according to the Euro Ewing 88 protocol (less intensive than the standard protocol).
The treatment consisted of five bimonthly courses of induction chemotherapy, consisting of cyclophosphamide at 150 mg/m$^2$ for seven days, followed by doxorubicin at 35 mg/m$^2$ on Day 8. After this induction, surgery was performed with margins of at least 5 mm, which were negative. Radiological evaluation revealed no suspicious mass, and no additional radiotherapy was conducted. Maintenance chemotherapy was initiated consisting of two phases. The first period included vincristine at 1.5 mg/m$^2$ weekly for 11 weeks and actinomycin every two weeks for up to six doses. The second period comprised six courses of cyclophosphamide and doxorubicin, similar to the induction scheme [1]. There was no evidence of disease progression one year after the diagnosis.
ES, or primitive neuroectodermal tumour (PNET), is mostly a primary tumour arising from bone or soft tissues. pCES is a very rare condition, with approximately 150 cases reported to date [1-3]. Most cases are observed in young adult female patients [3]. The lesion presents as a dermal or hypodermic circumscribed mobile nodule with a size <5 cm (1-12 cm), but clinical presentations may be heterogeneous. The most common locations are the extremities and trunk [3, 4].
Histopathological diagnosis of ES is tricky, requiring immunohistochemistry and molecular biological investigations to exclude other conditions associated with undifferentiated mesenchymal cells. CD99 antibody is not specific to ES and can be expressed in haematological malignancies, carcinomas, and sarcomas. However, the combination of cytoplasmic granular PAS positivity of tumour cells (Ewing sarcoma cells are rich in glycogen) and a cell membrane CD99 positive stain is highly suggestive of Ewing sarcoma [5].
The diagnosis needs to be confirmed by real-time polymerase chain reaction (RT-PCR) or FISH in order to detect gene translocations involving *ESWR1*, such as *EWSR1-FLI1* fusion [4-6]. To date, approximately 20 different fusions involving the *EWSR1* gene have been identified, four of which were more often associated with ES, involving *FLI1*, *ERG*, *FEV* and *ETV1/4* [5, 7].
In some rare cases, genes other than *EWSR1*, such as the *FUS* (fused in sarcoma) gene and other fusion partners, are involved [5].
There are no specific recommendations for treating pCES. The classic approach involves extensive surgery, radiotherapy when full surgical excision is impossible, and multi-drug chemotherapy according to the standard Euro-Ewing protocol. This treatment causes severe acute and late toxicities.
Considering the good prognosis of localized pCES and in order to reduce the risk of severe chemotherapy-related toxicity, some authors [3, 8] have proposed investigation of a less intensive chemotherapy regimen for localized disease. Indeed, pCES has a more favourable prognosis than bone ES [8, 9]. The 10-year survival probability has been estimated at 91% for pCES [8], compared to a five-year overall survival of 68% for localized bone ES [10].
The well-defined character of the lesion, small tumour size, and early detection probably contribute to the better prognosis [1-3, 8]. Further studies are required to support the use of less intensive chemotherapy combined with surgery as the treatment option with the best benefit/risk ratio for localized pCES. ■

**Disclosure.** *Financial support: none. Conflicts of interest: none*

[1] Department of Dermatology,
[2] Department of Pediatric Hematology and Oncology,
[3] Department of Pathology,
Cliniques Universitaires Saint-Luc, Brussels, Belgium
<valerie.dekeuleneer@uclouvain.be>

**Valérie DEKEULENEER[1]**
**Paméla EL NEMNOM[1]**
**Jeanne VERVIER[1]**
**Bénédicte BRICHARD[2]**
**Jordan LIBERT[3]**
**Pascal VAN EECKHOUT[3]**
**Liliane MAROT[3]**
**Dominique TENNSTEDT[1]**
**Gabriel LEVY[2]**
**Maëlle DE VILLE DE GOYET[2]**
**Cécile BOULANGER[2]**

**1.** Oberlin O, Deley MC, Bui BN, *et al.* Prognostic factors in localized Ewing's tumours and peripheral neuroectodermal tumours: the third study of the French Society of Paediatric Oncology (EW88 study). *Br J Cancer* 2001; 85: 1646-54.
**2.** Collier AB III, Simpson L, Monteleone P. Cutaneous Ewing sarcoma: report of 2 cases and literature review of presentation, treatment, and outcome of 76 other reported cases. *J Pediatr Hematol Oncol* 2011; 33: 631-4.
**3.** Di Giannatale A, Frezza AM, Le Deley MC, *et al.* Primary cutaneous and subcutaneous Ewing sarcoma. *Pediatr Blood Cancer* 2015; 62: 1555-61.
**4.** Molina-Ruiz AM, Busam KJ. Primary cutaneous Ewing sarcoma with EWSR1-ERG fusion. *J Cutan Pathol* 2016; 43: 729-34.
**5.** Kilpatrick SE, Reith JD, Rubin B. Ewing sarcoma and the history of similar and possibly related small round cell tumors: from whence have we come and where are we going? *Adv Anat Pathol* 2018; 25: 314-26.
**6.** Valente A, Tull J, Zhang S. Utility of fluorescence in situ hybridization in sub-classifying high-grade sarcomas: a study of 40 cases using break-apart probes of *EWSR1, FOXA1A, SS18* and *DDIT3* genes. *J Solid Tumors* 2012; 2: 2-9.
**7.** Cantile L, Marra L, Franco R, *et al.* Molecular detection and targeting of *EWSR1* fusion transcripts in soft tissue tumors. *Med Oncol* 2013; 30: 412.

**8.** Delaplace M, Lhommet C, de Pinieux G, *et al*. Primary cutaneous Ewing sarcoma: a systematic review focused on treatment and outcome. *Br J Dermatol* 2012; 166: 721-6.
**9.** Omori M, Ueno M, Ogawa M, Nagano T. Primary cutaneous extra skeletal Ewing's sarcoma/PNET: possibility of better prognosis than deep ES/PNET. *Eur J Dermatol* 2014; 24: 126-7.
**10.** Esiashvili N, Goodman M, Marcus RB Jr.. Changes in incidence and survival of Ewing sarcoma patients over the past 3 decades: surveillance epidemiology and end results data. *J Pediatr Hematol Oncol* 2008; 30: 425-30.

doi:10.1684/ejd.2018.3477

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