EWSR1::NFATC2-rearranged vascular anomaly arising in early childhood with morphologic atypia

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BACKGROUND

- *EWSR1*::*NFATC2*-rearranged tumors constitute an emerging spectrum of disease entities.
- Solitary bone cysts in the young and vascular malformations/hemangiomas of the bone in elderly patients have been reported to harbor *EWSR1::NFATC2* rearrangements and display benign behavior.
- *EWSR1::NFATC2* fusion-positive round cell sarcomas are a recently described subtype of "Ewing family" tumors with highly aggressive behavior and poor response to chemotherapy.
- A recent cohort of five adult patients with epithelioid vascular lesions harboring *EWSR1::NFATC2* rearrangements was described with cytologic atypia, including a distinct morphology comprised of alternating vasoformative and solid growth and mild to moderate nuclear pleomorphism.

CASE SUMMARY

- An 11-year-old female presented an extensive history of vertebral bony pathology.
- At 2 years of age, the patient presented with an L4 vertebral fracture with pathology showing a fibrovascular lesion with hemosiderin deposition.
- At 6, 8, and 10 years of age, sequential biopsies of a progressive L4 vertebral mass resulted in the diagnosis of a benign vascular malformation. **(Fig. 1)**
- At the most recent presentation, imaging revealed a 4.4 x 4.8 x 7.4 cm mass expansile into the retroperitoneum.
- Grossly, the mass was red-brown, lobulated, and firm, with cut surfaces demonstrating bony tissue with marked hemorrhage. **(Fig. 2)**
- Histologically, the tumor contained large thin- and thick-walled vascular structures with foci of intraluminal endothelial cell proliferation and epithelioid endothelial cells with atypical mitoses **(Fig. 3a-c).**
- Immunohistochemically, intraluminal spindle cells were CD31+ (**Fig. 3d),** CD34- **(Fig. 3e),** and Prox1+ **(Fig. 3f).** Chromogranin, CD56, panCK, EMA, BCL-2, CD99, NKX2.2, P53, myogenin, Phox2b, Glut-1, HMB-45, HHV-8, S-100, CAMTA1, and TFE3 were negative. BAF47/INI1 was retained. Ki-67 was focally increased with associated epithelioid cells.
- NGS RNA sequencing revealed an *EWSR1::NFATC2* fusion, later confirmed by breakapart *EWSR1* FISH **(Fig. 3g)**.
- The patient is currently disease free 6 months after bulk resection and is maintained on sirolimus therapy.

RESULTS

Figure 1. Timeline of disease course and imaging studies

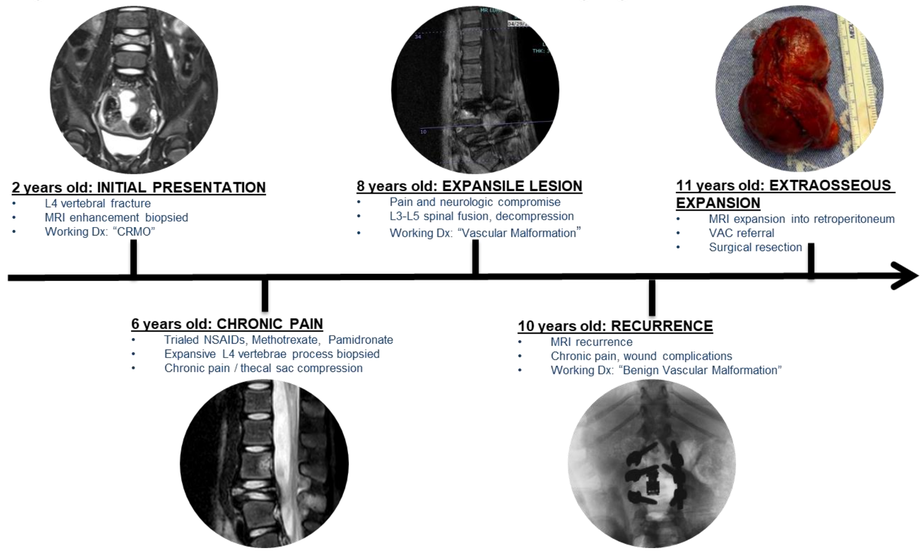


Figure 2. Gross pathology.

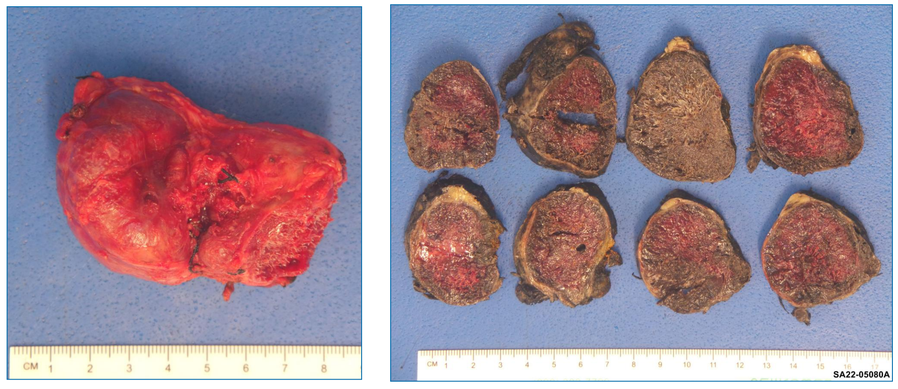
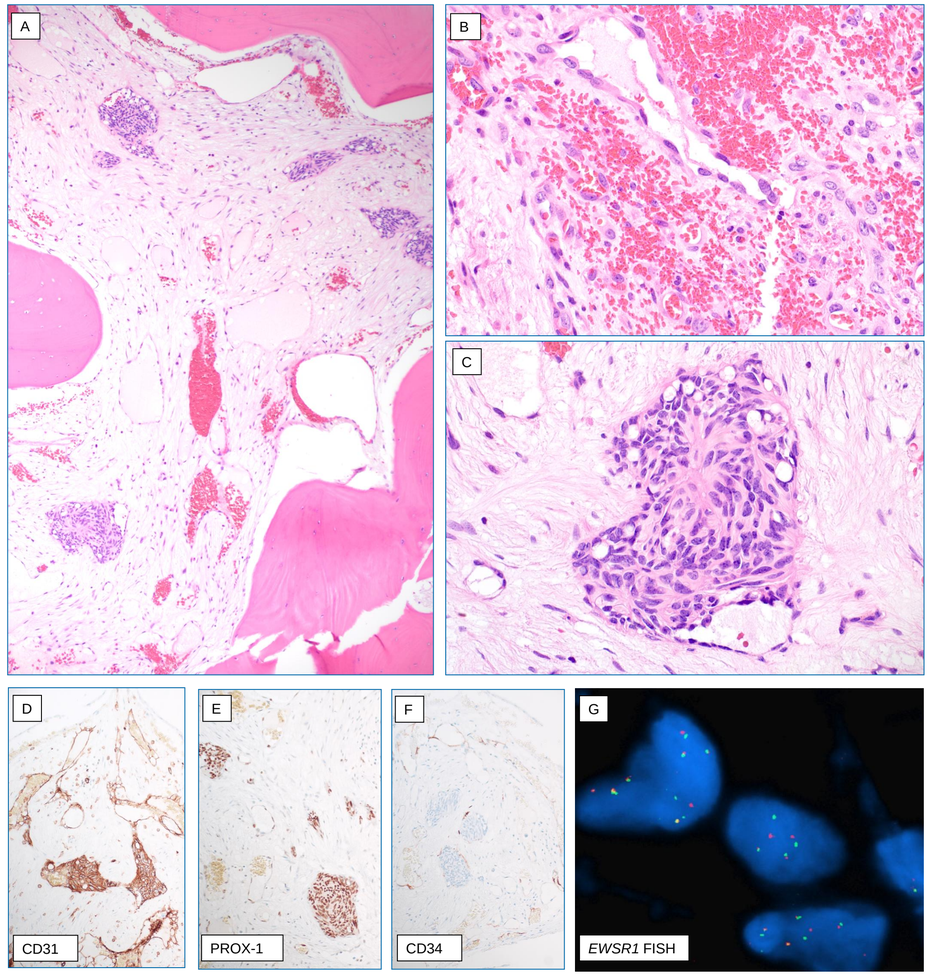


Figure 3. Microscopic pathology and cytogenetics studies.



DISCUSSION

- The findings are consistent with a vascular anomaly with *EWSR1::NFAT2C* rearrangement, scattered proliferative epithelioid endothelial cell clusters, and rare atypical mitoses.
- The patient's very early age at initial presentation and epithelioid and intravascular endothelial proliferations represent a unique pediatric presentation of an *EWSR1::NFATC*-rearranged epithelioid vascular tumor with apparent aggressive behavior.

REFERENCES

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