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Collaboration that builds better understanding in epithelioid sarcoma

Identifying epithelioid sarcoma (ES): QUICK REFERENCE GUIDE

This resource is for informational purposes only and is not intended to serve as a diagnostic tool or medical advice. It does not provide a comprehensive overview of all diagnostic options for ES. Healthcare professionals should rely on their clinical judgment and consult relevant guidelines or specialists when evaluating and diagnosing ES.

ES is a rare, aggressive cancer that may mimic benign and malignant conditions[1-3]

Most commonly affects young adults, with a median age of 27 years, but can occur at any age[1-3]

Twice as common in men as in women[1,2]

Commonly occurs on distal extremities but can arise almost anywhere in the body[1-3]

Early recognition may be critical

ES is **aggressive**,[1-4] with a **recurrence rate of 40%-50%**[5,6] and **metastasis rates of about 50%**[5,6]

Unlike many sarcomas, ES may **metastasize to regional lymph nodes** and **spread through the lymphatic system**, often reaching the **lungs**, **bones**, and **brain**[1-3]

Slow-growing lump[1-3]

Recurrence[1-3]

Metastasis[1-3]

Prompt specialist referral may improve outcomes by enabling earlier diagnosis and treatment[1,7-11]

ES is rare but serious.[1-3] Early recognition and specialist referral may be critical for improving patient outcomes[1,7-11]

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Recognizing ES can be challenging,[1-3,7,8] often leading to delayed diagnosis[8-12]

There are two distinct ES subtypes that vary in presentation, morphology, and prognosis[1-4,13-15]

Distal ES

Location: Subcutaneous or deep dermal mass in distal extremities, particularly fingers and hands[1-3,13,14]

Incidence: More common[2,13]

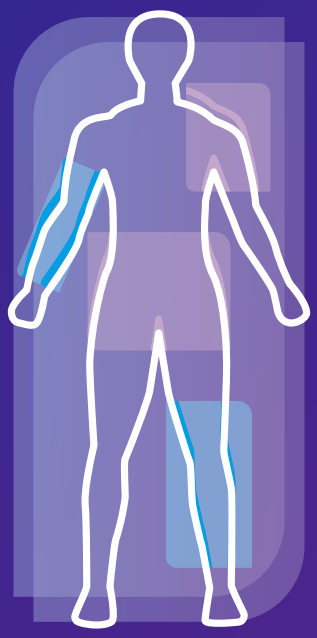
Age group: Typically occurs in younger patients (20-40 years)[2-4,13,14]

Sex: Male-to-female ratio 2:1[1,2,4]

Presentation: A superficial, slow-growing solid nodule or cluster of nodules, which may become ulcerated.[13] As the tumor invades, it compresses tendon sheaths and neurovascular bundles, causing pain, paresthesia, and restricted movement[8]

Behavior: Less aggressive with lower recurrence and metastasis rates, leading to a better prognosis and lower mortality compared to proximal ES[3,13,14]

Growth pattern: Nodular or lobular structure with central necrosis, surrounded by polygonal epithelioid cells with abundant eosinophilic cytoplasm, creating a granuloma-like appearance[1,2,13,14]



Proximal ES

Location: Deep, infiltrating soft-tissue mass/masses in proximal limbs, trunk, pelvis, perineum, and genital tract[1-3,13,14]

Incidence: Less common, making up about one-third of all ES cases[2,13]

Age group: Can affect older patients (20-65 years)[2-4,13,14]

Sex: Male to female ratio 1.6:1[4]

Presentation: Non-specific tissue masses develop deep in otherwise healthy tissue.[13] Commonly associated with hemorrhage and necrosis.[13] As the tumor progresses, it may be associated with site-specific symptoms and organ dysfunction[15]

Behavior: More aggressive than distal ES, with a higher rate of recurrence, earlier metastases and worse overall survival[3,4,13,14]

Growth pattern: Cellular nodules with increased cytologic pleomorphism, nuclear atypia, and rhabdoid morphology, characterized by prominent nucleoli[1,2,13,14]

Diagnostic challenges arise from several factors, which can lead to treatment delays and adversely impact outcomes[7-12]

Rarity of disease:
Makes up <1% of all soft tissue sarcomas[1,3,4]

Non-specific symptoms:
May resemble a benign lump, potentially leading to initial oversight[1-3,7,8,13]

Misdiagnosis risk:
Clinical and pathological features often mimic a number of benign and malignant conditions[1-3,7,8,13]

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ES signs and symptoms depend on tumor location and can vary widely[3]

Physical signs

Typical presentation

Distal ES

- Commonly occurs on distal extremities (hands, forearms, feet)[1-3,13,14]
- Superficial, slow-growing nodules, typically painless;[1,2,4,13,14] can also arise as deep-seated, slow-growing tumors[8]
- Typically <5 cm but can be larger[1,2]

Proximal ES

- Commonly occurs on proximal limbs, limb girdles, and midline trunk[1-3,13,14]
- Deep, infiltrating soft-tissue masses that commonly present with deeper tissue invasion[4,13,14]
- Can grow up to 20 cm[2,3,13,14]

Skin changes

- Overlying skin may have a shiny, gray-tan appearance[2]
- Superficial bleeding, necrosis, and ulceration may occur[2,3,13,14]

Symptoms

Pain or discomfort
May be painless initially but can cause discomfort as it grows; it may also cause pain sooner, depending on location (for example, near joints)[1-3,7,8,14]

Neurological symptoms
Localized growth can damage surrounding tissues, nerves, and blood vessels, and compression of nearby nerves or vessels can cause numbness, tingling, or weakness[1,8,13,14]

Tumor site-specific symptoms
Depending on the location, patients may experience bleeding, pain, or organ dysfunction[3,7,15]

Act fast: Early identification of ES may improve outcomes[7-11]

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Consider referring a patient for a sarcoma specialist evaluation

Key questions to consider when evaluating a suspicious lesion

1. **Onset:** Was the lesion sudden or gradual in appearance?
   Epithelioid sarcoma typically presents as a slow-growing, nodular lesion[1]
2. **Growth rate:** Is the lesion growing quickly, or is it stable?
   ES lesions often enlarge slowly over time, developing a multinodular appearance[1]
3. **History of trauma:** Has there been any history of injury or trauma to the area?
   ES can develop in areas with or without obvious trauma, but past injuries should still be considered[1,2]
4. **Neurovascular symptoms:** Is there any numbness, tingling, or weakness in the affected area?
   Compression of nerves can lead to neurological symptoms[8]
5. **Signs of pulmonary metastasis:** Has there been any new onset of cough, hemoptysis, or breathing difficulty?
   Metastasis to the lungs is common, and these symptoms may indicate advanced disease[1]

Seek support from a specialist sarcoma center if you observe:[16,17]

Lesion size >5 cm

Recent growth

Deep location

Pain

Any one of these four warning signs may warrant referral to a specialist sarcoma center[16,17]

When in doubt, consult a sarcoma specialist.[11,16-20]
Delays in diagnosis may worsen prognosis[7-11]

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References

1. Needs T, Fillman EP. Epithelioid sarcoma. Updated 2 July, 2024. Available at https://www.ncbi.nlm.nih.gov/books/NBK532911/. Accessed February 2025.
2. Czarnecka AM, Sobczuk P, Kostrzanowski M, et al. Epithelioid sarcoma - from genetics to clinical practice. *Cancers*. 2020;12:2112.
3. Czarnecka AM. Epithelioid sarcoma. *NOWOTWORY J Oncol*. 2023;73:154-161.
4. Del Savio E, Maestro R. Beyond SMARCB1 loss: Recent insights into the pathobiology of epithelioid sarcoma. *Cells*. 2022;11(17):2626.
5. de Visscher SA, van Ginkel RJ, Wobbes T, et al. Epithelioid sarcoma: Still an only surgically curable disease. *Cancer*. 2006;107(3):606-612.
6. Halling AC, Wollan PC, Pritchard DJ, et al. Epithelioid sarcoma: A clinicopathologic review of 55 cases. *Mayo Clin Proc*. 1996;71(7):636-642.
7. Zegarra Buitron E, Vidal Panduro DA, Morales Luna D. Clinicopathological characteristics, treatment, and survival in patients diagnosed with proximal-type epithelioid sarcoma: A case report and systematic review. *Cureus*. 2022;14(12):e32962.
8. Alexander L. Epithelioid sarcoma of upper extremity: Diagnostic dilemma with therapeutic challenges. *Cureus*. 2021;13(3):e14156.
9. Soomers V, Husson O, Young R, et al. The sarcoma diagnostic interval: A systematic review on length, contributing factors and patient outcomes. *ESMO Open*. 2020;5(1):e000592.
10. Younger E, Husson O, Bennister L, et al. Age-related sarcoma patient experience: Results from a national survey in England. *BMC Cancer*. 2018;18(1):991.
11. Recommendations from the Epithelioid Sarcoma Collaborative: A white paper. Available at https://www.jons-online.com/issues/2021/september-2021-vol-12-no-9/3914-recommendations-from-the-epithelioid-sarcoma-collaborative-a-white-paper. Accessed February 2025.
12. Martin S, Clark SE, Gerrand C, et al. Patients' experiences of a sarcoma diagnosis: A process mapping exercise of diagnostic pathways. *Cancers (Basel)*. 2023;15(15):3946.
13. Krotewicz M, Czarnecka AM, Błoński P, et al. Distal and proximal epithelioid sarcoma—differences in diagnosis and similarities in treatment. *Oncol Clin Pract*. 2024;99119.
14. Li Y, Cao G, Tao X, et al. Clinicopathologic features of epithelioid sarcoma: Report of seventeen cases and review of literature. *Int J Clin Exp Pathol*. 2019;12(8):3042-3048.
15. Ahmad Z, Stanazai Q, Wright S, et al. Primary pleural epithelioid sarcoma of the proximal type: A diagnostic and therapeutic challenge. *Transl Lung Cancer Res*. 2019;8(5):700-705.
16. Hayes AJ, Nixon IF, Strauss DC, et al. UK guidelines for the management of soft tissue sarcomas. *Br J Cancer*. 2025;132(1):11-31.
17. Gronchi A, Miah AB, Dei Tos AP, et al. Soft tissue and visceral sarcomas: ESMO-EURACAN-GENTURIS Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2021;32(11):1348-1365.
18. National Cancer Institute. Soft tissue sarcoma treatment (PDQ®)-health professional version. Available at https://www.cancer.gov/types/soft-tissue-sarcoma/hp/adult-soft-tissue-treatment-pdq. Accessed February 2025.
19. von Mehren M, Kane JM III, Bui MM, et al. Soft tissue sarcoma, Version 1.2021, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2020;18(12):1604-1612.
20. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Soft tissue sarcoma. Version 4.2024 — November 21, 2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed February 2025.

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