DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
JOINT BASE SAN ANTONIO - LACKLAND TEXAS

31 JULY 2017

MEMORANDUM FOR SGVT
ATTN: CAPT SIERRA MUSICK

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

Your paper, entitled **Chondroblastic Osteosarcoma Presenting as a Pulmonary Embolism** presented at/published to **Archives of Pathology, College of American Pathologists CAP17 The Pathologists' Meeting, Gaylord National, Maryland, October 8-11 2017** in accordance with MDWI 41-108, has been approved and assigned local file #**17298.**

Pertinent biographic information (name of author(s) title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.

Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are a 59 MDW staff member, we can forward your request for funds to the designated Wing POC at the Chief Scientist's Office, Ms. Alice Houy, office phone: 210-292-8029; email address: alice.houy.civ@mail.mil.

Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

Linda Steel-Goodwin

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

INSTRUCTIONS

USE ONLY THE MOST CURRENT 59 MDW FORM 3039 LOCATED ON AF E-PUBLISHING

1. The author must complete page two of this form:
   a. In Section 2, add the funding source for your study [e.g., 59 MDW CRD Graduate Health Sciences Education (GHSE) (SG5 O&M); SG5 R&D; Tri-Service Nursing Research Program (TSNRP); Defense Medical Research & Development Program (DMRDP); NIH; Congressionally Directed Medical Research Program (CDMRP) ; Grants; etc.]

   b. In Section 2, there may be funding available for journal costs, if your department is not paying for figures, tables or photographs for your publication. Please state "YES" or "NO" in Section 2 of the form, if you need publication funding support.

2. Print your name, rank/grade, sign and date the form in the author's signature block or use an electronic signature.

3. Attach a copy of the 59 MDW IRB or IACUC approval letter for the research related study. If this is a technical publication/presentation, state the type (e.g. case report, QA/QI study, program evaluation study, informational report/briefing, etc.) in the "Protocol Title" box.

4. Attach a copy of your abstract, paper, poster and other supporting documentation.

5. Save and forward, via email, the processing form and all supporting documentation to your unit commander, program director or immediate supervisor for review/approval.

6. On page 2, have either your unit commander, program director or immediate supervisor:
   a. Print their name, rank/grade, title; sign and date the form in the approving authority's signature block or use an electronic signature.

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8. The 59 CRD/Publications and Presentations Section will route the request form to clinical investigations, 502 ISG/JAC (Ethics Review) and Public Affairs (59 MDW/PA) for review and then forward you a final letter of approval or disapproval.

9. Once your manuscript, poster or presentation has been approved for a one-time public release, you may proceed with your publication or presentation submission activities, as stated on this form. **Note:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.

10. If your manuscript is accepted for scientific publication, please contact the 59 CRD/Publications and Presentations Section at 292-7141. This information is reported to the 59 MDW/CC. All medical research or technical information publications/presentations must be reported to the Defense Technical Information Center (DITC). See 59 MDWI 41-108, *Presentation and Publication of Medical and Technical Papers,* for additional information.

11. The Joint Ethics Regulation (JER) DoD 5500.07-R, *Standards of Conduct*, provides standards of ethical conduct for all DoD personnel and their interactions with other non-DoD entities, organizations, societies, conferences, etc. Part of the Form 3039 review and approval process includes a legal ethics review to address any potential conflicts related to DoD personnel participating in non-DoD sponsored conferences, professional meetings, publication/presentation disclosures to domestic and foreign audiences, DoD personnel accepting non-DoD contributions, awards, honoraria, gifts, etc. The specific circumstances for your presentation will determine whether a legal review is necessary. **If you (as the author) or your supervisor check "NO" in block 17 of the Form 3039, your research or technical documents will not be forwarded to the 502 ISG/JAC legal office for an ethics review.** To assist you in making this decision about whether to request a legal review, the following examples are provided as a guideline:

    For presentations before professional societies and like organizations, the 59 MDW Public Affairs Office (PAO) will provide the needed review to ensure proper disclaimers are included and the subject matter of the presentation does not create any cause for DoD concern.

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    If the sponsor of a conference or meeting is a non-DoD commercial entity or an entity seeking to do business with the government, then your presentation should have an ethics review.

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NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement:
"The views expressed are those of the [author(s)] [presenter(s)] and do not reflect the official views or policy of the Department of Defense or its Components"

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"The experiments reported herein were conducted according to the principles set forth in the National Institute of Health Publication No. 80-23, Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act of 1966, as amended."

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1. TO: CLINICAL RESEARCH	2. FROM: (Author's Name, Rank, Grade, Office Symbol)	3. GME/GHSE STUDENT:	4. PROTOCOL NUMBER:
	Sierra Musick, Capt, O-3, Sgvt	☒ YES ☐ NO	NA

5. PROTOCOL TITLE: (**NOTE:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.)

Case Report

6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED:

Chondroblastic Osteosarcoma Presenting as a Pulmonary Embolism

7. FUNDING RECEIVED FOR THIS STUDY? ☐ YES ☒ NO FUNDING SOURCE:

8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES: ☒ YES ☐ NO

9. IS THIS MATERIAL CLASSIFIED? ☐ YES ☒ NO

10. IS THIS MATERIAL SUBJECT TO ANY LEGAL RESTRICTIONS FOR PUBLICATION OR PRESENTATION THROUGH A COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT (CRADA), MATERIAL TRANSFER AGREEMENT (MTA), INTELLECTUAL PROPERTY RIGHTS AGREEMENT ETC.?
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☐ 11a. PUBLICATION/JOURNAL (List intended publication/journal.)

☒ 11b. PUBLISHED ABSTRACT (List intended journal.)
Archives of Pathology

☒ 11c. POSTER (To be demonstrated at meeting: name of meeting, city, state, and date of meeting.)
College of American Pathologists CAP17 The Pathologists' Meeting, Gaylord National, Maryland, October 8-11 2017

☐ 11d. PLATFORM PRESENTATION (At civilian institutions: name of meeting, state, and date of meting.)

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12. HAVE YOUR ATTACHED RESEARCH/TECHNICAL MATERIALS BEEN PREVIOUSLY APPROVED TO BE PUBLISHED/PRESENTED?
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13. EXPECTED DATE WHEN YOU WILL NEED THE CRD TO SUBMIT YOUR CLEARED PRESENTATION/PUBLICATION TO DTIC
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DATE	
September 01, 2017	

14. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email)	15. DUTY PHONE/PAGER NUMBER
Musick, Sierra, R., sierra.r.musick.mil@mail.mil	916-3181

16. AUTHORSHIP AND CO-AUTHOR(S) List in the order they will appear in the manuscript.

LAST NAME, FIRST NAME AND M.I.	GRADE/RANK	SQUADRON/GROUP/OFFICE SYMBOL	INSTITUTION (If not 59 MDW)
a. Primary/Corresponding Author Sierra Musick	O-3/Capt	959 MDG/CSP/Sgvt	
b. David T Lynch	O-4/Maj	959 MDG/CSP/Sgvt	
c. Gabriella Cardoza-Favarato	O-5/LtCol	959 MDG/CSP/Sgvt	
d.			
e.			

17. IS A 502 ISG/JAC ETHICS REVIEW REQUIRED (JER DOD 5500.07-R)? ☒ YES ☐ NO

I CERTIFY ANY HUMAN OR ANIMAL RESEARCH RELATED STUDIES WERE APPROVED AND PERFORMED IN STRICT ACCORDANCE WITH 32 CFR 219, AFMAN 40-401_IP, AND 59 MDWI 41-108. I HAVE READ THE FINAL VERSION OF THE ATTACHED MATERIAL AND CERTIFY THAT IT IS AN ACCURATE MANUSCRIPT FOR PUBLICATION AND/OR PRESENTATION.

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PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

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TO: Clinical Research Division 59 MDW/CRD Contact 292-7141 for email instructions.	24. DATE RECEIVED July 27, 2017	25. ASSIGNED PROCESSING REQUEST FILE NUMBER 17298
26. DATE REVIEWED 28 Jul 2017		27. DATE FORWARDED TO 502 ISG/JAC

28. AUTHOR CONTACTED FOR RECOMMENDED OR NECESSARY CHANGES: ☒ NO ☐ YES If yes, give date. _____ ☐ N/A

29. COMMENTS ☒ APPROVED ☐ DISAPPROVED

The abstract is approved.

30. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	31. REVIEWER SIGNATURE	32. DATE
Rocky Calcote, PhD, Clinical Research Administrator	CALCOTE.ROCKY.D.1178245844 Digitally signed by CALCOTE.ROCKY.D.1178245844 DN: c=US, o=U.S. Government, ou=DoD, ou=PKI, ou=USAF, cn=CALCOTE.ROCKY.D.1178245844 Date: 2017.07.28 10:32:29 -05'00'	

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4th ENDORSEMENT (59 MDW/SGVU Use Only)

45. DATE RECEIVED	46. SENIOR AUTHOR NOTIFIED BY PHONE OF APPROVAL OR DISAPPROVAL ☐ YES ☐ NO ☐ COULD NOT BE REACHED ☐ LEFT MESSAGE

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48. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	49. REVIEWER SIGNATURE	50. DATE

Chondroblastic Osteosarcoma Presenting as a Pulmonary Embolism

Authors: Sierra Musick, MD, David T Lynch, MD, Gabriella Cardoza-Favarato, MD

Introduction

Osteosarcomas are more common in younger adults; however, extraskeletal osteosarcomas are more likely in older adults. Extraskeletal osteosarcoma is defined as a malignant mesenchymal neoplasm that produces varying amounts of osteoid, immature bone or chondroid matrix, located in the soft tissue without connection to the skeleton. The retroperitoneum, deep muscles of the thigh, pelvis and shoulder girdles are common locations. These tumors tend to be highly aggressive with only a 20% average 5-year survival rate .

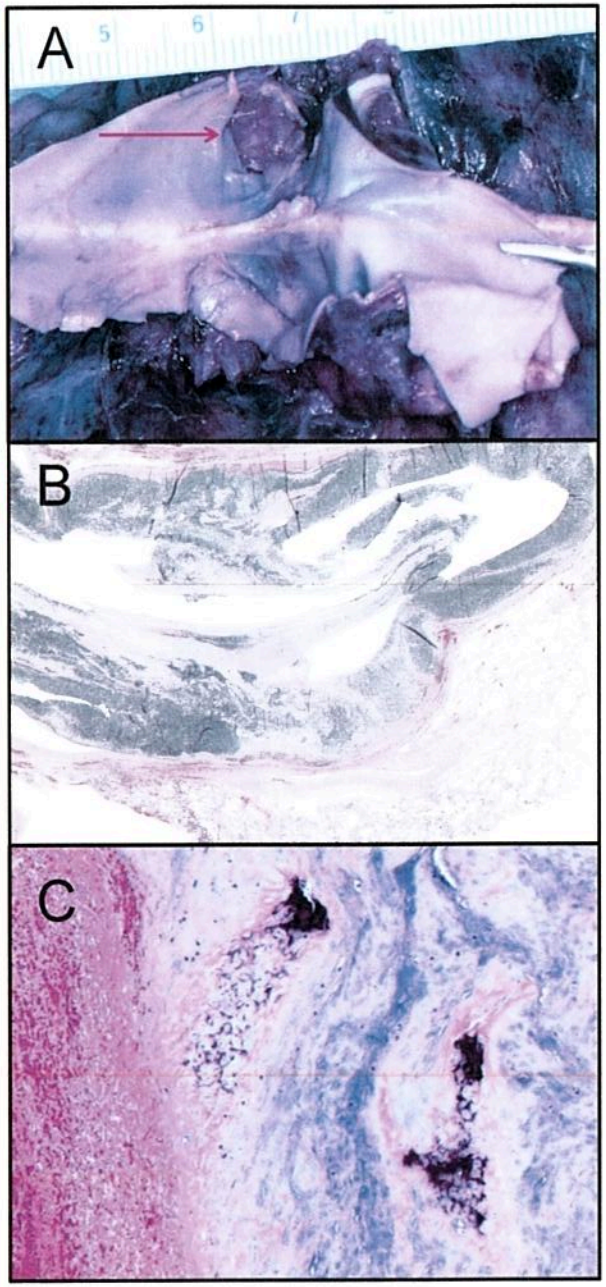
These lesions are thought to represent the progression of soft tissue or epithelial malignancies. Rarely, extraskeletal osteosarcomas have been known to occur in the heart and the pulmonary arteries, the latter of which can present as a pulmonary embolism. They are highly aggressive and commonly metastasize to the lungs. We report a case of a woman found to have chondroblastic osteosarcoma in her heart and pulmonary arteries.

Case Report

A previously healthy 63-year-old woman presented with several weeks of shortness of breath and fatigue was diagnosed with a massive pulmonary embolism. On imaging, she was diagnosed with occlusion of the right segmental pulmonary arteries and multifocal pulmonary infarcts of the right lung. A biopsy of the suspected pulmonary embolism showed minute fragments of thrombus with admixed inflammatory cells, but was negative for malignancy. The clinical team's suspicion for malignancy persisted given the lack of response to anticoagulation and thrombolysis. However, a full body positron emission tomography (PET) scan did not reveal any malignant foci.

Upon pulmonary artery embolectomy, a mass was identified. The pulmonary artery mass frozen specimen was a white-tan-red glistening multinodular firm mass with a cut surface revealing solid and cystic areas with a gelatinous appearance. Histologically, it was reported as an atypical osteocartilaginous neoplasm, which prompted a unilateral pneumonectomy. Grossly, the pneumonectomy specimen demonstrated the mass occluding multiple large and small pulmonary vessels (Figure A).

On permanent sections, a neoplasm in the pulmonary artery and lung showed lobules of neoplastic cartilage with surrounding and intervening spindle cells, osteoid and bone (Figure B and C). The mitotic rate was greater than 20/10 HPFs and the histological grade was 3. Direct chest wall extension and lympho-vascular invasion were also identified. Necrotic chondroid tissue was found in the tricuspid valve vegetation. Undifferentiated malignant spindle cells were found in the pulmonic valve vegetation. Further imaging and physical exam revealed no other site of tumor.



Pathology

Figure A. Gross examination of pneumonectomy specimen with large pulmonary vessel containing the mass (red arrow).

Figure B. Hematoxylin and eosin histopathologic evaluation demonstrating the neoplasm in the pulmonary artery.

Figure C. Hematoxylin and eosin histopathologic evaluation showsing neoplastic spindle cells, osteoid and bone next to an area of hemorrhage and necrosis.

Discussion

Extraskeletal osteosarcoma comprise only 1% to 2% of all soft tissue sarcomas (3). They typically occur in patients older than 40 years of age with no clear sex predilection. Common locations include the lower extremity, particularly the thigh, the upper extremities and the retroperitoneum. Rarely, extraskeletal osteosarcomas have been known to occur in the heart, pulmonary pleura, pulmonary arteries, mediastinum, mesentery, omentum and esophagus. Those arising in the lung are especially rare, with the first case report in 1933 (1).

Production of osteoid or bone by cytological malignant cells is required for diagnosis (2). Histologically, extraskeletal osteosarcomas resemble undifferentiated pleomorphic sarcomas with the addition of osteoid. Atypical cartilage, if present, rarely predominates, as was the case in this patient's tumor. Given the hypothesis that these lesions represent the progression of soft tissue or epithelial malignancies, it is most likely that this patient's tumor arose from the pulmonary arteries and subsequently spread to the cardiac valves in the form of vegetations. Alternatively, this tumor could have been a metastasis. However, this is unlikely given the full body positron emission tomography (PET) scan did not reveal any malignant foci. The differential diagnosis should include other malignant tumors that may have metaplastic bone formation, such as epithelioid sarcoma, synovial sarcoma, mixed malignant mullerian tumor (MMMT) and malignant melanoma. The patient had no history of malignancy and therefore was diagnosed with intravascular and parenchymal metastatic chrondorblastic osteosarcoma with the suspected site of origin being the lung vasculature. This case highlights an uncommon presentation of a diagnostically challenging case of chondroblastic osteosarcoma.

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Osteosarcomas are more common in younger adults; however, extraskeletal osteosarcomas are more likely in older adults. Rarely, osteosarcomas have been known to occur in the heart and the pulmonary arteries, the latter of which can present as a pulmonary embolism. They are highly aggressive and commonly metastasize to the lungs. We report a case of a woman found to have chondroblastic osteosarcoma in her heart and pulmonary arteries. A previously healthy 63-year-old woman presented with several weeks of shortness of breath and fatigue was diagnosed with a massive pulmonary embolism. On imaging, she was diagnosed with occlusion of the right segmental pulmonary arteries and multifocal pulmonary infarcts of the right lung. A biopsy of the suspected pulmonary embolism showed minute fragments of thrombus with admixed inflammatory cells, but was negative for malignancy. Upon pulmonary artery embolectomy, a mass was identified. The pulmonary artery mass frozen specimen was a white-tan-red glistening multinodular firm mass with a cut surface revealing solid and cystic areas with a gelatinous appearance. On permanent sections, a neoplasm in the pulmonary artery and lung showed lobules of neoplastic cartilage with surrounding and intervening spindle cells and osteoid (see image). Necrotic chondroid tissue was found in the tricuspid valve vegetation. Undifferentiated malignant spindle cells were found in the pulmonic valve vegetation. Imaging and physical exam revealed no other site of tumor. This case highlights an uncommon presentation of a diagnostically challenging case of chondroblastic osteosarcoma.

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