



Case Report

Traumatic tumor hemorrhage of inflammatory myofibroblastic tumor of the lung

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ABSTRACT

A 23-year-old female with a history of idiopathic epilepsy was found to have a right chest cavity shadow in a school health checkup 5 years before. CT revealed a thin-walled cavity lesion in the right middle lobe containing a ball-like mass, showing air crescent sign. After falling due to a seizure, she was transported by ambulance and admitted. CT revealed diffuse ground-glass opacities throughout the right lung field. Bronchoscopy revealed bloody bronchial alveolar lavage fluid. Due to the tumor hemorrhage, an elective simple right middle lobe resection was performed without complications. The initial immunohistochemical staining was negative for ALK using ALK1 clone; however, subsequent staining of ALK by D5F3 and 5A4 clone was positive. Immunostaining findings led to a diagnosis of inflammatory myofibroblastic tumor. The patient remains under regular observation and has experienced no recurrence over the 6-year postoperative period. This case contains two different points: the first is that a cavity lesion of inflammatory myofibroblastic tumor may cause traumatic bleeding and should be treated with caution; the second is that attention should be paid to differences in stainability among clones when diagnosing inflammatory myofibroblastic tumor.

1. Introduction

In cases of minimal change in chest abnormal shadows, prolonged observation may be required. In cases where a diagnosis cannot be made of tumor lesions through examination, such as using bronchoscopy, surgical resection is planned; however, balancing the expected diagnosis and the invasiveness of surgery is challenging. Younger individuals generally have a lower likelihood of malignant diseases; therefore, if no changes are observed in imaging and the patient wishes to undergo observation without surgery, continued observation can be selected [1].

The present case involved a rare clinical course of an inflammatory myofibroblastic tumor (IMT) during observation. We report the rare case of IMT with the difficulties in histopathological diagnosis.

2. Case presentation

A 23-year-old female with a history of idiopathic epilepsy was found to have a right chest cavity shadow in a school health checkup 5 years before. CT revealed a thin-walled cavity lesion in the right middle lobe containing a ball-like mass, showing air crescent sign (Fig. 1A). Initial examinations yielded nonspecific results: she was negative for tuberculosis specific IFN- γ , Cryptococcus antigen, Candida antigen, Aspergillus antigen, β -D-glucan, and CEA 0.8, SCC 0.9, CYFRA 0.8, and ProGRP 43.2. A follow-up CT scan in three months revealed that the lesion had remained almost unchanged, with only slight movement of its contents. Considering the

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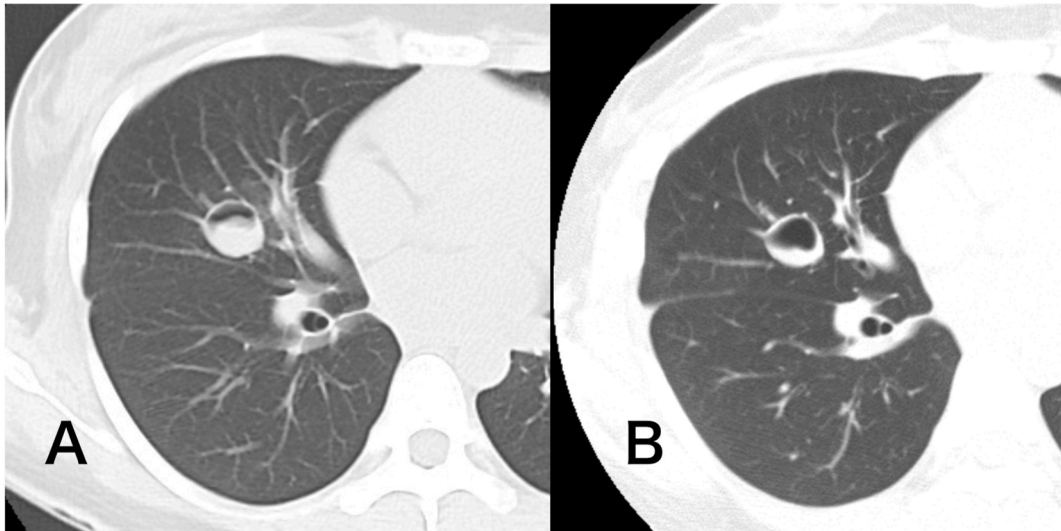


Fig. 1. CT findings at initial examination and 3 years later. (A) CT with 5 mm slice thickness at initial examination shows a cavity lesion measuring 18 mm in the right middle lobe S4 region. The air crescent sign is present, but the wall is thin without halo sign, indicating strong inflammation unlikely. (B) CT with 3 mm slice thickness at 3 years later. The internal mass was seemed to have a little fluidity, and its shape had changed slightly each CT scan.

mild thickening of the cavity wall and the absence of significant malignancy indicators, malignancy was not strongly suspected. In the cases of solitary cavitory lesions excluding lung apical bullae, the possibility of neoplastic disease must be considered, and a histological diagnosis is deemed crucial. We suggested either a bronchoscopic biopsy or a surgical lung biopsy, she declined our proposal and opted for follow-up CT observation. The CT scans showed no significant changes in the lesion for years (Fig. 1B).

Four years had passed since the initial visit, the patient fell due to a seizure and was transported by ambulance and admitted to our hospital. Although the seizure had subsided, CT revealed diffuse ground-glass opacities throughout the right lung field and in part of the left lower lobe (Fig. 2). Bronchoscopy revealed bloody bronchial alveolar lavage fluid. Since the tumor hemorrhage was temporary and the hemoptysis ceased, emergency surgery was not performed, and the patient was discharged on 9 hospital day.

Due to the tumor hemorrhage, an elective surgical treatment was planned (Fig. 3). The patient was re-admitted and right middle lobe resection was performed without complications. She was discharged after a successful postoperative course. Histopathological

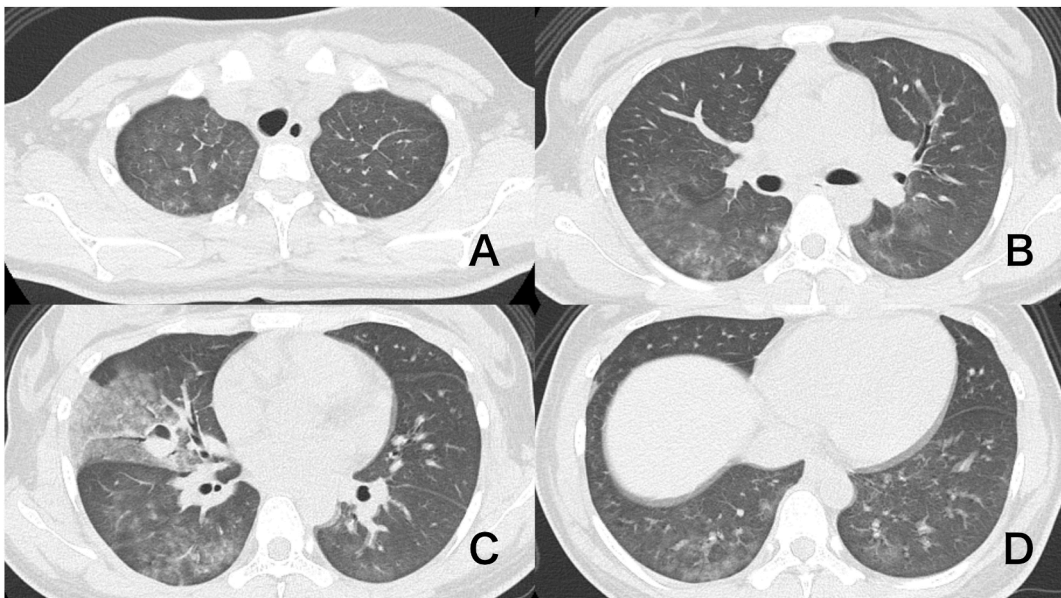


Fig. 2. CT findings of traumatic tumor hemorrhage. (A)–(D) CT with 1 mm slice thickness at hemorrhage onset. Diffuse ground-glass opacities were seen throughout the right lung field and in a part of the left lower lobe, which is prominent around the tumor and in the right middle lobe, strongly suggesting bleeding from the tumor. Additionally, the shadow is stronger on the peripheral side of the tumor, and considering that the tumor communicates with the peripheral bronchus, it is conceivable that bleeding within the tumor has dispersed peripherally through the bronchus.

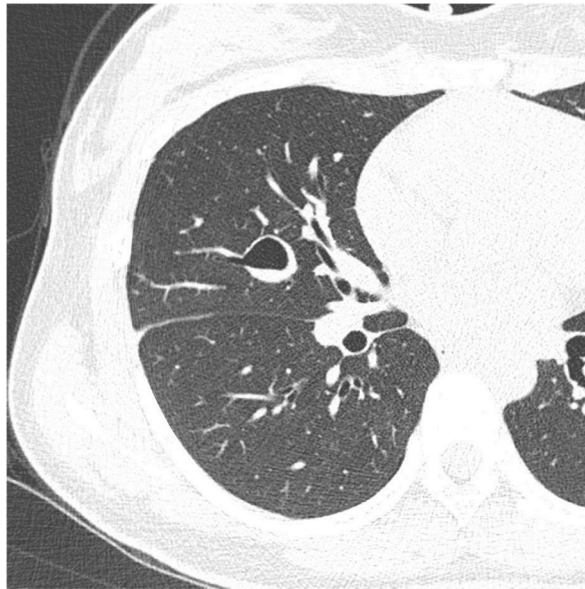


Fig. 3. CT findings of preoperative scan 1 month after traumatic tumor hemorrhage CT with 1 mm slice thickness shows the abnormal shadow due to bleeding has disappeared, and there are no significant changes in the tumor. The internal content has further decreased.

examination revealed spindle-shaped cells with a clear cytoplasm forming a sheet-like structure with few mitotic counts, and there were no prominent atypical features. Infiltration of inflammatory cells such as lymphocytes and neutrophils was observed, with some staghorn-like vessels (Fig. 4). IMT, solitary fibrous tumor, pulmonary sclerosing hemangioma, and perivascular epithelioid cell tumor were considered differential diagnoses. Immunohistochemical (IHC) staining was positive for vimentin and SMA. Staining for CD34, c-kit, STAT6, HMB45, TTF-1, IgG4, and ALK was negative (Fig. 5). Since a definitive diagnosis could not be reached, an external consultation was conducted and staining showed positive for ALK, which differed from our findings. As they used D5F3 clone, whereas

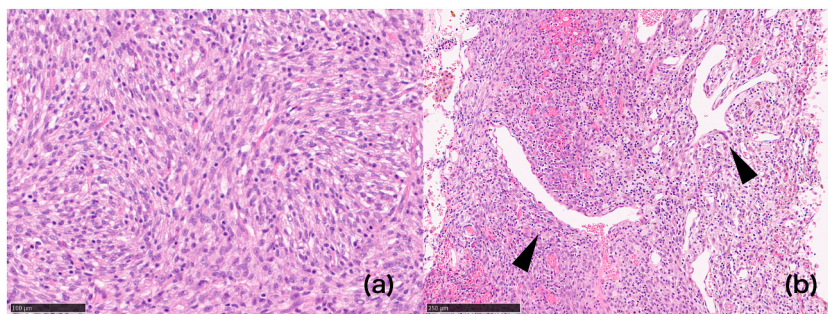


Fig. 4. Histopathological findings of the tumor (a) (Hematoxylin and eosin [HE] staining, x200) Histopathological examination reveals spindle-shaped cells with a clear cytoplasm forming a sheet-like structure. (b) (HE staining, x100) Staghorn-like vessels (black arrowhead).

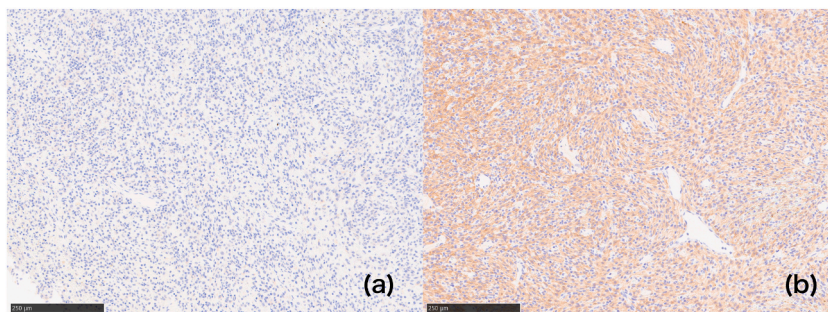


Fig. 5. Difference in immunohistochemical stainability (a) Negative for ALK1 clone. (b) Positive for 5A4 clone.

we used ALK1 clone in our hospital, upon receipt of the results, experimental staining with the 5A4 clone was performed for confirmation and the results were positive (Fig. 5). The immunostaining results led to a diagnosis of IMT.

The patient remains under regular observation and has experienced no recurrence over the 6-year postoperative period.

3. Discussion

IMT is a rare malignant tumor that predominantly affects young individuals and can occur in various locations besides the lungs [2]. The most consistent pathologic feature of IMT is a proliferation of spindle cells associated with a variably dense polymorphic infiltrate of mononuclear inflammatory cells [3]. In recent years, surgical treatment was performed for five cases of IMT over a three-year period in Japan. During this period, surgeries for primary lung cancer exceeded 130 thousand cases [4–6]. Approximately 70 % of IMT patients are asymptomatic, according to a recent study [7]; however, previous studies reported that respiratory symptoms, such as cough and hemoptysis, are common [8,9]. Surgical complete resection is the optimal treatment for this condition. However, in cases where complete resection is not possible, Crizotinib has been reported as a treatment option [10].

The imaging features of IMTs are heterogeneous. Narla et al. [11] reported that they often present as solitary, well-demarcated nodules or infiltrative shadows. There were 66 articles describing IMT included “cavitary” or “cavity” in PubMed. Among these, 6 IMT cases in 3 reports described cavity lesion in the thoracic region [12–14]. The imaging findings presented in these articles appear to be cavities caused by necrosis. In our case, the slightly thickened wall of the cavitary tumor lesion was composed of tumor components, but there was no associated necrosis histologically.

In cases of cystic lung cancer, which is relatively common compared to IMT, the etiology of cystic lesions varies with multiple hypotheses [15]. Based on this report, the expansion of the cavitary lesion is most likely due to the tumor directly destruction of pulmonary alveoli. As for the formation of the cavity, it might be related to the involvement of relatively large bronchi which may serve as air passage. Differentiating this disease based on imaging may be difficult, the presence of a solitary cavitary lesion with a thin wall, especially if it does not seemed to be so-called bullae, might suggest a malignant lesion including IMT over infectious diseases.

The present case was asymptomatic and discovered through a regular checkup; however, it exhibited a rare event of traumatic tumor bleeding during the observation period. There are no previous reports of traumatic tumor hemorrhage of the lung; however, traumatic bleeding has been reported in hydatid cyst [16]. The bleeding in this case resulted from a fall due to a seizure. The likelihood of a patient losing consciousness and falling in daily life is considered low; however, considering that young patients may engage in sports involving physical impact, it is advisable to consider the possibility of bleeding due to daily activities while observing cavitary lesions. Appropriate surgical indications should also be considered.

Histologically diagnosing this case was challenging. IMT has been reported to be ALK-positive in 72.5 % of cases by IHC staining [17]. In this case, the initial IHC staining using ALK1 clone (DakoCytomation, Denmark) was ALK-negative, posing diagnostic difficulties. Consultation with an external institution revealed positivity using the D5F3 clone, suggesting IMT. Subsequent staining with the 5A4 clone (Nichirei Biosciences Inc., Japan) at our hospital yielded positive results and we diagnosed IMT. Since control tissues were also stained with ALK1 clone, issues with the reagent or procedure are unlikely. While ALK-negative IMT is reported to have a higher frequency of metastasis compared to ALK-positive tumors [18], the role of ALK positivity is crucial as a supplementary diagnostic tool for accurate prognosis prediction. There is a report that D5F3 is superior to ALK1 in lung adenocarcinoma [19]; however, there is no report on staining details for IMT. Our findings suggest that it is necessary to pay attention to clone differences and detection methods when performing conventional IHC staining.

4. Conclusion

When IMT presents as a cavity lesion, the possibility of tumor hemorrhage should be considered. Although an accurate ALK result is important for diagnosis and prognosis prediction, caution is required due to potential difficulties in staining.

CRedit authorship contribution statement

Takashi Yamashita: Conceptualization, Data curation, Formal analysis, Investigation, Supervision, Validation, Writing – original draft. **Yuta Matsubayashi:** Data curation, Formal analysis, Investigation, Writing – review & editing. **Takahiro Mochizuki:** Investigation, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviation

IMT inflammatory myofibroblastic tumor
IHC immunohistochemical

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References

- [1] M.K. Gould, J. Donington, W.R. Lynch, P.J. Mazzone, D.E. Midthun, D.P. Naidich, R.S. Wiener, Evaluation of individuals with pulmonary nodules: when is it lung cancer? *Chest* 143 (2013) e93S–e120S, <https://doi.org/10.1378/chest.12-2351>.
- [2] C.M. Coffin, P.A. Humphrey, L.P. Dehner, Extrapulmonary inflammatory myofibroblastic tumor: a clinical and pathological survey, *Semin. Diagn. Pathol.* 15 (1998) 85–101. <http://www.ncbi.nlm.nih.gov/pubmed/9606801>.
- [3] L.M. Lai, M.B. McCarville, P. Kirby, S.C.S. Kao, T. Moritani, E. Clark, K. Ishigami, A. Bahrami, Y. Sato, Shedding light on inflammatory pseudotumor in children: spotlight on inflammatory myofibroblastic tumor, *Pediatr. Radiol.* 45 (2015) 1738–1752, <https://doi.org/10.1007/s00247-015-3360-6>.
- [4] H. Shimizu, M. Okada, A. Tangoku, Y. Doki, S. Endo, H. Fukuda, Y. Hirata, H. Iwata, J. Kobayashi, H. Kumamaru, H. Miyata, N. Motomura, S. Natsugoe, S. Ozawa, Y. Saiki, A. Saito, H. Saji, Y. Sato, T. Taketani, K. Tanemoto, W. Tatsuishi, Y. Toh, H. Tsukahara, M. Watanabe, H. Yamamoto, K. Yokoi, Y. Okita, Thoracic and cardiovascular surgeries in Japan during 2017, *Gen. Thorac. Cardiovasc. Surg.* 68 (2020) 414–449, <https://doi.org/10.1007/s11748-020-01298-2>.
- [5] H. Shimizu, M. Okada, Y. Toh, Y. Doki, S. Endo, H. Fukuda, Y. Hirata, H. Iwata, J. Kobayashi, H. Kumamaru, H. Miyata, N. Motomura, S. Natsugoe, S. Ozawa, Y. Saiki, A. Saito, H. Saji, Y. Sato, T. Taketani, K. Tanemoto, A. Tangoku, W. Tatsuishi, H. Tsukahara, M. Watanabe, H. Yamamoto, K. Minatoya, K. Yokoi, Y. Okita, M. Tsuchida, Y. Sawa, Thoracic and cardiovascular surgeries in Japan during 2018, *Gen. Thorac. Cardiovasc. Surg.* 69 (2021) 179–212, <https://doi.org/10.1007/s11748-020-01460-w>.
- [6] K. Minatoya, Y. Sato, Y. Toh, T. Abe, S. Endo, Y. Hirata, M. Ishida, H. Iwata, T. Kamei, N. Kawaharada, S. Kawamoto, K. Kohno, H. Kumamaru, G. Matsumiya, N. Motomura, R. Nakahara, M. Okada, H. Saji, A. Saito, H. Shimizu, K. Suzuki, H. Takemura, T. Taketani, H. Takeuchi, W. Tatsuishi, H. Yamamoto, T. Yasuda, M. Watanabe, N. Yoshimura, M. Tsuchida, Y. Sawa, Thoracic and cardiovascular surgeries in Japan during 2019, *Gen. Thorac. Cardiovasc. Surg.* (2023), <https://doi.org/10.1007/s11748-023-01945-4>.
- [7] A.E.S. Sagar, C.A. Jimenez, V.R. Shannon, Clinical and histopathologic correlates and management strategies for inflammatory myofibroblastic tumor of the lung. A case series and review of the literature, *Med. Oncol.* 35 (2018) 102, <https://doi.org/10.1007/s12032-018-1161-0>.
- [8] R.J. Cerfolio, M.S. Allen, A.G. Nascimento, C. Deschamps, V.F. Trastek, D.L. Miller, P.C. Pairolero, Inflammatory pseudotumors of the lung, *Ann. Thorac. Surg.* 67 (1999) 933–936, [https://doi.org/10.1016/S0003-4975\(99\)00155-1](https://doi.org/10.1016/S0003-4975(99)00155-1).
- [9] G.A. Agrons, M.L. Rosado-de-Christenson, W.M. Kirejczyk, R.M. Conran, J.T. Stocker, Pulmonary inflammatory pseudotumor: radiologic features, *Radiology* 206 (1998) 511–518, <https://doi.org/10.1148/radiology.206.2.9457206>.
- [10] J.E. Butrynski, D.R. D'Adamo, J.L. Hornick, P. Dal Cin, C.R. Antonescu, S.C. Jhanwar, M. Ladanyi, M. Capelletti, S.J. Rodig, N. Ramaiya, E.L. Kwak, J.W. Clark, K.D. Wilner, J.G. Christensen, P.A. Jänne, R.G. Maki, G.D. Demetri, G.I. Shapiro, Crizotinib in ALK-rearranged inflammatory myofibroblastic tumor, *N. Engl. J. Med.* 363 (2010) 1727–1733, <https://doi.org/10.1056/NEJMoa1007056>.
- [11] L. Das Narla, B. Newman, S.S. Spottswood, S. Narla, R. Kolli, Inflammatory pseudotumor, *RadioGraphics.* 23 (2003) 719–729, <https://doi.org/10.1148/rg.233025073>.
- [12] S. Eldaabossi, L. Maghmoul, E. Lotfy, A. Antar, Y. Elghoneimy, H. Aljawad, A. Ghoneim, Common Presentation of Uncommon Disease: inflammatory myofibroblastic tumor of the lung, case report, *Respir. Med. Case. Rep.* 37 (2022) 101656, <https://doi.org/10.1016/j.rmcr.2022.101656>.
- [13] J. Arunachalam, H. Radhakrishnan, H. Patel, G.K. Johal, G.D. Medarametla, A. Sheikh, S.N. Mahmood, V. Shah, D. Patel, N. Changawala, Inflammatory myofibroblastic tumor mimicking a cavitary lesion in the lung: a case report and a comprehensive literature review, *Cureus* (2022), <https://doi.org/10.7759/cureus.29193>.
- [14] J. Wu, H. Zhu, K. Li, C.-Y. Yuan, Y.-F. Wang, G.-M. Lu, Imaging observations of pulmonary inflammatory myofibroblastic tumors in patients over 40 years old, *Oncol. Lett.* 9 (2015) 1877–1884, <https://doi.org/10.3892/ol.2015.2923>.
- [15] X. Tang, G. Liu, X. Tan, C. Liu, J. Xiang, Y. Jiang, Solitary multicystic lesion lung cancer: two case reports and review of the literature, *BMC Pulm. Med.* 21 (2021) 368, <https://doi.org/10.1186/s12890-021-01729-7>.
- [16] J. Couniot, Traumatic rupture of a hydatid cyst of the lung: secondary hemoptyses, pneumonectomy, *Afr. Fr. Chir.* 3 (1953) 345–348. <http://www.ncbi.nlm.nih.gov/pubmed/13104270>.
- [17] H. Yamamoto, Y. Nozaki, K. Kohashi, I. Kinoshita, Y. Oda, Diagnostic utility of pan-Trk immunohistochemistry for inflammatory myofibroblastic tumours, *Histopathology* 76 (2020) 774–778, <https://doi.org/10.1111/his.14010>.
- [18] C.M. Coffin, J.L. Hornick, C.D.M. Fletcher, Inflammatory myofibroblastic tumor, *Am. J. Surg. Pathol.* 31 (2007) 509–520, <https://doi.org/10.1097/01.pas.0000213393.57322.c7>.
- [19] M. Mino-Kenudson, L.R. Chirieac, K. Law, J.L. Hornick, N. Lindeman, E.J. Mark, D.W. Cohen, B.E. Johnson, P.A. Jänne, A.J. Iafrate, S.J. Rodig, A novel, highly sensitive antibody allows for the routine detection of ALK-rearranged lung adenocarcinomas by standard immunohistochemistry, *Clin. Cancer Res.* 16 (2010) 1561–1571, <https://doi.org/10.1158/1078-0432.CCR-09-2845>.