



Unexpected Dramatic Response of Pretreated Invasive Thymic Malignancies on Pemetrexed-Case Report and Review of Current Treatment Modalities

PDF (Size:1282KB) PP. 107-115 **DOI:** 10.4236/ojrd.2012.24016

Author(s)

Priscilla Raman, Veerle Surmont

ABSTRACT

Thymomas are rare and usually slowly growing tumors, originating from the epithelial layer of the thymus. Prognosis depends on the extent of invasion of adjacent tissues whereby multimodality treatment including surgery with or without adjuvant chemoradiotherapy is the preferred approach for locally advanced thymomas. For metastatic thymomas, only few chemotherapeutic options are available. We report 2 cases of patients with metastatic thymic malignancies with a dramatic response on pemetrexed treatment. The choice for this antifolate therapy is based upon a small series. Because metastatic thymic neoplasm is a rare disease, large randomised trials are not feasible. Case reports on the treatment of these malignancies are very important and can provide readers with the opportunity to deal with rare diseases.

KEYWORDS

Thymoma; Pemetrexed; Thymic Carcinoma; Combined Modality Therapy; Molecular Targeted Therapy

Cite this paper

P. Raman and V. Surmont, "Unexpected Dramatic Response of Pretreated Invasive Thymic Malignancies on Pemetrexed-Case Report and Review of Current Treatment Modalities," *Open Journal of Respiratory Diseases*, Vol. 2 No. 4, 2012, pp. 107-115. doi: 10.4236/ojrd.2012.24016.

References

- [1] W. K. de Jong, J. L. G. Blaauwgeers, M Schaapveld, et al., "Thymic Epithelial Tumours: A Population-Based Study of the Incidence, Diagnostic Procedures and Therapy," *European Journal of Cancer*, Vol. 44, No. 1, 2008, pp 123-130. doi:10.1016/j.ejca.2007.11.004
- [2] P. Engel, A. Marx and H. K. Müller-Hermelink, "Thymic tumours in Denmark. A Retrospective Study of 213 Cases from 1970-1993," *Pathology—Research and Practice*, Vol. 195, No. 8, 1999, pp. 565-570. doi:10.1016/S0344-0338(99)80006-5
- [3] J. V. Souadjan, P Enriquez, M. N. Silverstein and J. M. Pépin, "The Spectrum of Diseases Associated with Thymoma. Coincidence or Syndrome?" *Archives of Internal Medicine*, Vol. 134, No. 2, 1974, pp. 374-379. doi:10.1001/archinte.1974.00320200184029
- [4] E. N. Dessimis, "The Biology of Pure Red Cell Aplasia," *Semin Hematol*, Vol. 28, No. 4, 1991, pp. 275-284.
- [5] P. E. Tarr, M. C. Sneller, L. J. Mechanic, et al., "Infections in Patients with Immunodeficiency with Thymoma (Good Syndrome). Report of 5 Cases and Review of the Literature," *Medicine (Baltimore)*, Vol. 80, No. 2, 2001, pp. 123-133. doi:10.1097/00005792-200103000-00005
- [6] T. Y. Eng, C. D. Fuller, J. Jagirdar, et al., "Thymic Carcinoma: State of the Art Review," *International Journal of Radiation Oncology, Biology, Physics*, Vol. 59, No. 3, 2004, pp. 654-664. doi:10.1016/j.ijrobp.2003.11.021
- [7] J. E. Lewis, M. R. Wick, B. W. Scheithauer, et al., "Thymoma. A Clinicopathologic Review," *Cancer*, Vol. 60, No. 11, 1987, pp. 2727-2743. doi:10.1002/1097-0142(19871201)60:11<2727::AID-CNCR28101420111>3.0.CO;2-1

OJRD Subscription

Most popular papers in OJRD

About OJRD News

Frequently Asked Questions

Recommend to Peers

Recommend to Library

Contact Us

Downloads:	5,319
------------	-------

Visits:	33,057
---------	--------

Sponsors >>

- [8] F. C. Detterbeck, " Clinical Value of the WHO Classification System of Thymoma," *The Annals of Thoracic Surgery*, Vol. 81, No. 6, 2006, pp. 2328-2334. doi:10.1016/j.athoracsur.2005.11.067
- [9] A. Masaoka, Y. Monden, K. Nakahara and T. Tanicka, " Follow-Up Study of Thymomas with Special Reference to Their Clinical Stages," *Cancer*, Vol. 48, No. 11, 1981, pp. 2485-2492. doi:10.1002/1097-0142(19811201)48:11<2485::AID-CNCR2820481123>3.0.CO;2-R
- [10] K. Kondo and Y. Monden, " Therapy of Thymic Epithelial Tumors: A Clinical Study of 1320 Patients from Japan," *The Annals of Thoracic Surgery*, Vol. 76, No. 3, 2003, pp 878-884. doi:10.1016/S0003-4975(03)00555-1
- [11] " NCCN Clinical Practice Guidelines in Oncology," 2010. http://www.nccn.org/professionals/physician_gls/PDF/thymic.pdf
- [12] P. Str?bel, R. Bargou, A. Wolff, et al., " Sunitinib in Metastatic Thymic Carcinomas: Laboratory Findings and Initial Clinical Experience," *British Journal of Cancer*, Vol. 103, No. 2, 2010, pp. 196-200. doi:10.1038/sj.bjc.6605740
- [13] G. Bisagni, G. Rossi, A. Cavazza, et al., " Long lasting Response to the Multikinase Inhibitor Bay 43-9006 (Sorafenib) in a Heavily Pretreated Metastatic Thymic Carcinoma," *Journal of Thoracic Oncology*, Vol. 4, No. 6, 2009, pp. 773-775. doi:10.1097/JTO.0b013e3181a52e25
- [14] X. F. Li, Q. Chen, W. X. Huang and Y. B. Ye, " Response to Sorafenib in Cisplatin-Resistant Thymic Carcinoma: A Case Report," *Medical Oncology*, Vol. 26, No. 2, 2009, pp 157-160. doi:10.1007/s12032-008-9100-0
- [15] F. C. Detterbeck and A. M. Parsons, " Thymic Tumors," *The Annals of Thoracic Surgery*, Vol. 77, No. 5, 2004, pp. 1860-1869. doi:10.1016/j.athoracsur.2003.10.001
- [16] E. Davenport and R. A. Malthaner, " The Role of Surgery in the Management of Thymoma: A Systematic Review," *The Annals of Thoracic Surgery*, Vol. 86, No. 2, 2008, pp. 673-684. doi:10.1016/j.athoracsur.2008.03.055
- [17] P. Str?bel, A. Bauer, B. Puppe, et al., " Tumor Recurrence and Survival in Patients Treated for Thymomas and Thymic Squamous Cell Carcinomas: A Retrospective Analysis," *Journal of Clinical Oncology*, Vol. 22, No. 8, 2004, pp 1501-1509. doi:10.1200/JCO.2004.10.113
- [18] J.-F. Regnard, P. Magdeleinat, C. Dromer, et al., " Prognostic Factors and Long-Term Results after Thymoma Resection: A Series of 307 Patients," *The Journal of Thoracic and Cardiovascular Surgery*, Vol. 112, No. 2, 1996, pp. 376-384. doi:10.1016/S0022-5223(96)70265-9
- [19] M. Okumura, S. Miyoshi, Y. Takeuchi, et al., " Results of Surgical Treatment of Thymomas with Special Reference to the Involved Organs," *The Journal of Thoracic and Cardiovascular Surgery*, Vol. 117, No. 3, 1999, pp. 605613. doi:10.1016/S0022-5223(99)70343-0
- [20] T. Murakawa, J. Nakajima, T. Kohno, et al., " Results from Surgical Treatment for Thymoma. 43 Years of Experience," *The Journal of Thoracic and Cardiovascular Surgery*, Vol. 48, No. 2, 2000, pp. 89-95. doi:10.1007/BF03218097
- [21] C. B. Falkson, A. Bezjak, G. Darling, et al., " The Management of Thymoma: A Systematic Review and Practice Guideline," *Journal of Thoracic Oncology*, Vol. 4, No. 7, 2009, pp. 911-919. doi:10.1097/JTO.0b013e3181a4b8e0
- [22] J. L. Port and R. J. Ginsberg, " Surgery for the Thymoma," *Chest Surgery Clinics of North America*, Vol. 11, No. 2, 2001, pp. 421-437.
- [23] Y. J. Cheng, J. S. Hsu and E. L. Kao, " Characteristics of Thymoma Successfully Resected by Videothorascopic Surgery," *Surgery Today*, Vol. 37, No. 3, 2007, pp. 192196. doi:10.1007/s00595-006-3383-6
- [24] A. Toker, J. Sonett, M. Zielinski, et al., " Standard Terms, Definitions and Policies for Minimally Invasive Resection of Thymoma," *Journal of Clinical Oncology*, Vol. 6, 2011, pp. S1739-1748.
- [25] J. A. Forquer, N. Rong, A. J. Fakiris, et al., " Postoperative Radiotherapy after Surgical Resection of Thymoma: Differing Roles in Localized and Regional Diseases," *International Journal of Radiation Oncology, Biology, Physics*, Vol. 76, No. 2, 2010, pp. 440-445. doi:10.1016/j.ijrobp.2009.02.016
- [26] K. Ogawa, T. Uno, T. Toita, et al., " Postoperative Radiotherapy for Patients with Completely

- [27] T. Utsumi, H. Shiono, Y. Kadota, et al., " Postoperative Radiation Therapy after Complete Resection of Thymoma Has Little Impact on Survival," Cancer, Vol. 115, No. 23, 2009, pp. 5413-5420. doi:10.1002/cncr.24618
- [28] S. Kaseda, H. Horinouchi, R. Kato, et al., " Treatment of Invasive Thymoma Using Low Dose and Extended-Field Irradiation Including Hemi-Thorax or Whole-Thorax," Kyobu Geka, Vol. 46, No. 1, 1993, pp. 31-40.
- [29] D. Gomez, R. Komaki, J. Yu, H. Ikushima and A. Bezjak, " Radiation Therapy Definitions and Reporting Guidelines for Thymic Malignancies," Journal of Thoracic Oncology, Vol. 6, No. 7, 2011, pp. S1743-S1748. doi:10.1097/JTO.0b013e31821ea60c
- [30] W. J. Curran, M. J. Kornstein, J. J. Brooks, et al., " Invasive Thymoma: The Role of Mediastinal Irradiation," Journal of Clinical Oncology, Vol. 6, No. 11, 1988, pp. 1722-1727.
- [31] E. S. Kim, J. B. Putnam, R. Komaki, et al., " Phase II Study of a Multidisciplinary Approach with Induction Chemotherapy, Followed by Surgical Resection, Radiation Therapy and Consolidation Chemotherapy for Unresectable Malignant Thymomas: Final Report," Lung Cancer, Vol. 44, No. 3, 2004, pp. 369-379. doi:10.1016/j.lungcan.2003.12.010
- [32] A. Berruti, P. Borasio, A. Gerbino, et al., " Primary Chemotherapy with Adriamycin, Cisplatin, Vincristine and Cyclophosphamide in Locally Advanced Thymomas: A Single Institution Experience," British Journal of Cancer, Vol. 81, No. 5, 1999, pp. 841-845. doi:10.1038/sj.bjc.6690773
- [33] P. J. Sr Loehrer, M. Chen, K. Kim, et al., " Cisplatin, Doxorubicin and Cyclophosphamide Plus Thoracic Radioation Therapy for Limited-Stage Unresectable Thymoma: An Intergroup Trial," Journal of Clinical Oncology, Vol. 15, No. 9, 1997, pp. 3093-3099.
- [34] " Lung Cancer Evidence-Based Series (EBS) and Practice Guidelines (PG) (Cancer Care Ontario Website)." <http://www.cancercare.on.ca/english/home/toolbox/qualityguidelines/diseasesite/lung-ebs/>
- [35] T. Evans and T. J. Lynch, " Role of Chemotherapy in the Management of Advanced Thymic Tumors," Seminars in Thoracic and Cardiovascular Surgery, Vol. 17, No. 1, 2005, pp. 41-50. doi:10.1053/j.semtcv.2004.11.003
- [36] G. Giaccone, A. Ardizzone, A. Kirkpatrick, et al., " Cisplatin and Etoposide Combination Chemotherapy for Locally Advanced or Metastatic Thymoma. A phase II Study of the European Organisation for Research and Treatment of Cancer Lung Cancer Cooperative Group," Journal of Clinical Oncology, Vol. 14, No. 3, 1996, pp. 814-820.
- [37] P. J. Sr Loehrer, K. Kim, S. C. Aisner, et al., " Cisplatin Plus Doxorubicin plus Cyclophosphamide in Metastatic or Recurrent Thymoma: Final Results of an Intergroup Trial. The Eastern Cooperative Oncology Group, SouthWest Oncology Group, and Southeastern Cancer Study Group," Journal of Clinical Oncology, Vol. 12, No. 6, 1994, pp. 1164-1168.
- [38] R. J. Kelly, I. Petrini, A. Rajan, Y. Wang and G. Giaccone, " Thymic Malignancies: From Clinical Management to Targeted Therapies," Journal of Clinical Oncology, Vol. 29, No. 36, 2011, pp. 4820-4827. doi:10.1200/JCO.2011.36.0487
- [39] N. Girard, RohitLal, P. Loehrer, et al., " Chemotherapy Definitions and Policies for Thymic Malignancies," Journal of Thoracic Oncology, Vol. 6, No. 7, 2011, pp. S1749-S1755. doi:10.1097/JTO.0b013e31821ea5f7
- [40] A. M. Cimpean, M. Raica, S. Encica, et al., " Immunohistochemical Expression of Vascular Endothelial Growth Factor A (VEGF) and Its Receptors (VEGFR1,2) in Normal and Pathological Conditions of the Human Thymus," Annals of Anatomy, Vol. 190, No. 3, 2008, pp. 238-245. doi:10.1016/j.aanat.2007.05.003
- [41] H. Sasaki, H. Yukie, Y. Kobayashi, et al., " Elevated Serum Vascular Endothelial Growth Factor and Basis Fibroblast Growth Factor Levels in Patients with Thymic Epithelial Neoplasms," Surgery Today, Vol. 31, No. 11, 2001, pp. 1038-1040. doi:10.1007/s005950170021
- [42] M. Tomita, Y. Matsuzaki, M. Edagawa, et al., " Correlation between Tumor Angiogenesis and Invasiveness in Thymic Epithelial Tumors," The Journal of Thoracic and Cardiovascular Surgery, Vol. 124, No. 3, 2002, pp. 493-498. doi:10.1067/mtc.2002.124389

- [43] G. Giaccone, A. Rajan, A. Berman, et al., " Phase II Study of Belinostat in Patients with Recurrent or Refractory Advanced Thymic Epithelial Tumors," *Journal of Clinical Oncology*, Vol. 29, No. 15, 2011, pp. 2052-2059. doi:10.1200/JCO.2010.32.4467
- [44] C. Kirkove, J. Berghmans, H. Noel, et al., " Dramatic Response of Recurrent Invasive Thymoma to High Doses of Corticosteroids," *Clinical Oncology*, Vol. 4, No. 1, 1992, pp. 64-66. doi:10.1016/S0936-6555(05)80783-6
- [45] C. Craven, P. K. Reddy, S. P. Ringel, et al., " Effect of Corticosteroids on the Thymus in Myasthenia Gravis," *Muscle Nerve*, Vol. 4, No. 5, 1981, pp. 425-428. doi:10.1002/mus.880040512
- [46] T. Reisine and G. I. Bell, " Molecular Biology of Somatostatin Receptors," *Endocrine Reviews*, Vol. 16, No. 4, 1995, pp. 427-442.
- [47] P. J. Sr Loehrer, W. Wang, D. H. Johnson, et al., " Octreotide Alone or with Prednisone in Patients with Advanced Thymoma and Thymic Carcinoma: An Eastern Cooperative Oncology Group Phase II Trial," *Journal of Clinical Oncology*, Vol. 22, No. 2, 2004, pp. 293-299. doi:10.1200/JCO.2004.02.047
- [48] N. Girard, J. Teruya-Feldstein, E. C. Payabyab, et al., " Insulin-Like Growth Factor-1 Receptor Expression in Thymic Malignancies," *Journal of Thoracic Oncology*, Vol. 5, No. 9, 2010, pp. 1439-1446. doi:10.1097/JTO.0b013e3181e392a8
- [49] P. Haluska, H. M. Shaw, G. N. Batzel, et al., " Phase I Dose Escalation Study of the Anti-Insulin-Like Growth Factor-I Receptor Monoclonal Antibody CP-751, 871 in Patients with Refractory Solid Tumors," *Clinical Cancer Research*, Vol. 13, No. 19, 2007, pp. 5834-5840. doi:10.1158/1078-0432.CCR-07-1118
- [50] C. Shih, V. J. Chen, L. S. Gosset, et al., " LY231514, a Pyrroro (2,3) Pyrimidine-Based Anti-Folate That Inhibits Multiple Folate-Requiring Enzymes," *Cancer Research*, Vol. 57, No. 6, 1997, pp. 1116-1123.
- [51] N. J. Vogelzang, J. J. Rusthoven, J. Symanowski, et al., " Phase III Study of Pemetrexed in Combination with Cisplatin Versus Cisplatin Alone in Patients with Malignant Pleural Mesothelioma," *Journal of Clinical Oncology*, Vol. 21, No. 14, 2003, pp. 2636-2644. doi:10.1200/JCO.2003.11.136
- [52] N. Hanna, F. A. Shepherd, F. V. Fossella, et al., " Randomized Phase III Trial of Pemetrexed versus Docetaxel in Patients with Non-Small-Cell Lung Cancer Previously Treated with Chemotherapy," *Journal of Clinical Oncology*, Vol. 22, No. 9, 2004, pp. 1589-1597. doi:10.1200/JCO.2004.08.163
- [53] G. V. Scagliotti, P. Parikh, J. vonPawel, et al., " Phase III Study Comparing Cisplatin Plus Gemcitabine with Cisplatin Plus Pemetrexed In Chemotherapy-Naive Patients with Advanced-Stage Non-Small-Cell Lung Cancer," *Journal of Clinical Oncology*, Vol. 26, No. 21, 2008, pp. 3543-3551. doi:10.1200/JCO.2007.15.0375
- [54] G. V. Scagliotti, N. Hanna, F. Fossella, et al., " The Differential Efficacy of Pemetrexed According to NSCLC Histology: A Review of Two Phase III Studies," *The Oncologist*, Vol. 14, No. 3, 2009, pp. 253-263. doi:10.1634/theoncologist.2008-0232
- [55] R. M. Schultz, V. J. Chen, J. R. Belwely, et al., " Biological Activity of the Multitargetedantifolate, Mta (Ly231514), in Human Cell Lines with Different Resistance Mechanisms to Antifolate Drugs," *Seminars in Oncology*, Vol. 26, No. 2 supplement 6, 1999, pp. 68-73.
- [56] E. Giovannetti, V. Mey, S. Nannizzi, et al., " Cellular and Pharmacogenetics Foundation of Synergistic Interaction of Pemetrexed and Gemcitabine in Human Non-SmallCell Lung Cancer Cells," *Molecular Pharmacology*, Vol. 68, No. 1, 2005, pp. 110-118.
- [57] P. Ceppi, M. Volante, S. Saviozzi, et al., " Squamous Cell Carcinoma of the Lung Compared with Other Histotypes Shows Higher Messenger RNA and Protein Levels for Thymidylate Synthase," *Cancer*, Vol. 107, No. 7, 2006, pp. 1589-1596. doi:10.1002/cncr.22208
- [58] P. Ceppi, M. Volante, A. Ferrero, et al., " Thymidylate Synthase Expression in Gastroenteropancreatic and Pulmonary Neuroendocrine Tumors," *Clinical Cancer Research*, Vol. 14, No. 4, 2008, pp. 1059-1064. doi:10.1158/1078-0432.CCR-07-1513
- [59] P. J. Loehrer, C. T. Yiannoutsos, S. Dropcho, et al., " A Phase II Trial of Pemetrexed in Patients with Recurrent Thymoma or Thymic Carcinoma," *Journal of Clinical Oncology*, Vol. 24, No. 18s, 2006.

