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33 with anaplastic transformation in an elderly woman.

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35 **CASE REPORT**

36 A 71- year- old female presented to our surgical department complaining of painful,
37 erythematous and ulcerated neck mass causing bleeding (figure 1). She also
38 complained of shortness of breath and generalized fatigue. Her medical history
39 included osteoporosis, hypertension and dyslipidemia. The history dates back to 5
40 years ago when she had noticed to have a cervical nodule during routine
41 examination for elective cholecystectomy. Chest radiograph at that time noticed a
42 well-defined nodule about 4 * 4 cm (figure 2). That pathological findings was ignored
43 by the patient till recently when that mass started to grow up, ulcerate and bleed.
44 Patient underwent incisional biopsy of the mass which turned to be metastatic
45 papillary carcinoma in cervical lymph node with extensive neoplastic infiltration of
46 skin and sub-cutaneous tissue by anaplastic tumor, giant cell type. A whole body
47 Computed tomography showed multiple metastatic lung nodules. The rest of the
48 body was free of metastasis. Multimodal therapeutic approaches were started
49 including debulking surgery (R2 resection), radiation to a biologically equivalent dose
50 and adjuvant chemotherapy with doxorubicin and docetaxel. Despite supportive
51 treatment her condition kept deteriorating and presented later with advanced necrotic
52 neck tumor that causing active bleeding (figure 3). At this moment the treatment
53 discontinued as per family request and had just curettage to alleviate the bleeding
54 process. After several weeks the tumor progressed rapidly to reach a huge size
55 (figure 4) and patient started to have dysphonia, dysphagia, and dyspnea.
56 Unfortunately patient subsequently died.

57

58 **DISCUSSION**

59 Anaplastic thyroid cancer (ATC) accounts for a small percentage of thyroid cancers
60 (1.6%) and ranks among the most aggressive and lethal solid tumors of all human
61 malignancies with a disease-specific mortality approaching 100% [1]. It accounts,
62 however, for 14 to 39% of thyroid cancer deaths [2]. The mean survival rate ranges
63 from 4 to 12 months [1].

64 Approximately half of patients at the time of diagnosis with ATC have evidence of
65 distant metastatic disease, which is represents a poor clinical prognostic factor that
66 predicts rapid disease progression and death [3]). Another 25% will develop distant
67 spread during the course of their disease [4].

68 It is well known that ATC does not arise de novo but rather considered part of the
69 natural history of untreated papillary thyroid carcinoma (PTC) or follicular carcinoma
70 and Hurthle cell tumors [1]. However some authors like Sam M et al, evaluate the
71 change in the cancer expression profile that occurs during the transformation of DTC
72 into ATC. They identified a panel of 3 upregulated markers (β -catenin [CTNNB1],
73 topoisomerase II- α [TOPO-II], and vascular endothelial growth factor [VEGF]) and 2
74 downregulated markers (thyroglobulin [TG], , Ecadherin [E-CAD]) seem to most
75 consistently differentiate ATC from DTC [4].

76 There is no definitely effective therapy exists for ATC even with aggressive
77 multimodal approach. A Research Consortium of Japan (ATCCJ) analyzed data from
78 a large cohort of 677 ATC patients to determine prognostic factors and treatment
79 outcomes for ATC. They found that only 15% of patients achieved long-term survival
80 exceeding 1 year after diagnosis and concluded that complete resection is
81 considered the cornerstone for longer survival, along with adjuvant radio-
82 chemotherapy [2].

83 A recent review reported success of combining external beam radiotherapy EBRT
84 (multiple small radiation doses that allow more than one radiation treatment a day)
85 with taxanes in anaplastic thyroid cancer. The local control rate was 60%, but the 2-
86 yr survival was only 9%. In only 24% was death attributable to local failure, reflecting
87 the high rate of distant metastatic disease that is unresponsive to chemotherapy [5].

88

89 CONCLUSION

90 In conclusion, we have described a case of anaplastic transformation of papillary
91 carcinoma with lung metastasis and we emphasized the aggressiveness and rapid
92 behavior of this tumor (it is not unusual for tumor volume to double over a week of
93 observation). Because of its rarity and rapidly fatal clinical course ATC has been
94 difficult to study and despite aggressive treatment, almost all affected individuals
95 eventually die of their disease.

96 **KEYWORDS**

97 Anaplastic tumor, Local advance, Fatal outcome.

98

99 **CONFLICT OF INTEREST**

100 No conflict of interest.

101

102 **AUTHOR'S CONTRIBUTIONS**

103 Houssam Abtar

104 Group 1- Substantial contributions to conception and design, Acquisition of data,
105 Analysis and interpretation of data,

106 Group 2- Drafting the article, revising it critically for important intellectual content,

107 Group 3- Final approval of the version to be published

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121 Group 2- Revising it critically for important intellectual content,

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140 **FIGURE LEGENDS**

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142 Figure 1 Right sided ulcerated neck mass causing erythema of the skin.

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144 Figure 2: Chest X-ray showed well-defined nodule 40.8*43.2 mm causing tracheal
145 deviation.

146

147 Figure 3: Advanced necrotic bleeding tumor extended outside the skin and involving
148 the surrounding tissue.

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150 Figure 4: Very ugly looking 15*15 cm tumor with areas of necrosis.

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159 **FIGURES**

160



161

162

163 Figure 1 Right sided ulcerated neck mass causing erythema of the skin.

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166

167 Figure 2: Chest X-ray showed well-defined cervical nodule 40.8*43.2 mm causing
168 tracheal deviation.



169

170

171 Figure 3: Advanced necrotic bleeding tumor extended outside the skin and involving
172 the surrounding tissue.

173



174

175

176 Figure 4: Very ugly looking 15*15 cm tumor with areas of necrosis.