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Resection for Internal Jugular Vein Thrombosis and Cervical Lymph Nodes' Involvement from Gastric Cancer

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Abstract. *Background/Aim: Thrombosis internal jugular vein (IJV) with cervical adenopathy, as first manifestation of gastric cancer is rare. We aimed to compare resection of the cervical mass followed by gastrectomy with gastrectomy alone. Patients and Methods: Nine patients presenting thrombosis of the IJV for gastric carcinoma were divided into two groups. Patients in group A (n=3) underwent anticoagulation treatment, gastrectomy and adjuvant treatment. Patients in group B (n=6) underwent resection of the cervical mass and internal jugular vein (radical neck dissection), and then gastrectomy and adjuvant treatment. Results: Median survival was 15.3 months in group A (range=11-19 months) and 31.2 months in group B (range=7-44 months) (p=0.11). Late cervical recurrence/ complications occurred in 2 patients in group A and none in group B (p=0.02). Conclusion: Resection of thrombosed IJV and satellite lymph nodes, due to a primary gastric cancer may contribute to diagnosis of the disease, limit pulmonary embolic complications and improve quality of life.*

Involvement of a distal site as first clinical sign of gastric cancer, although quite rare, is known and includes migratory trombophlebitis or Trousseau's syndrome (1) and metastasis to supraclavicular Virchow's node, known as Troisier's sign (2). The appearance of a cervical mass and swelling due to thrombosis if the internal jugular veinn (IJV) related to gastric carcinoma, has recently been the subject of isolated case reports (3-6) and treated with anticoagulation. The prognostic value of this sign is not well defined. There also is a lack of sufficient length follow-up to demonstrate whether simple anticoagulation or resection would be more appropriate for preventing further complications and cervical recurrence.

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We retrospectively reviewed our experience with the management of IJV thrombosis and cervical masses as first manifestation and distal localization of gastric cancer, in order to determine whether resection would improve survival, local control and quality of life.

Patients and Methods

From January 2000 to December 2019, 9 previously healthy patients, of whom 6 men of a mean age of 58 year, were admitted to an academic, tertiary care hospital and one associated centre of reference for oncologic research and care, for the diagnosis and treatment of an enlarging cervical mass associated with cervical swelling. All the patients gave their informed consent for all the proposed treatments and, as their clinical records were retrospectively reviewed for the study's purpose, institutional ethics committee's approval was waived. Clinical patients' data were entered into a database regularly updated during follow-up. The first appearance of the mass dated back to a mean time interval of 6 days (range=4-16 days). The mass was not associated with any subjective symptom in 6 cases, whereas it was associated with mild dysphagia in 2 cases, and with fever and pain in one case. Patients' diagnostic workup consisted of a complete CT-scan of the head, neck, chest and abdomen, followed by upper gastro-intestinal endoscopy. The CT-scan showed an isolated thrombosis of the IJV associated with thickening or an endoluminal mass arising from the gastric wall in 3 patients (group A) and an asymptomatic pulmonary thrombus in the inferior lobar division of the right pulmonary artery. In these patients, a subsequent endoscopy with biopsy confirmed the diagnosis of gastric adenocarcinoma. In the remaining 6 patients the cervical mass consisted of confluent cervical lymph nodes encasing an IJV with intraluminal thrombus of variable extension from the mastoid process to the confluence of the subclavian vein (group B) (Figure 1). In this latter group, a suspicious, synchronous thickening of the gastric wall together with adenopathy of various extension of the lymph nodes of the gastric region was evident in 4 patients, whereas it appeared with a delay of 2 and 3 months in the remaining 2 patients. One patient also presented asymptomatic emboli in the upper lobar segments of the left pulmonary artery. In group B, endoscopy with biopsy revealing gastric adenocarcinoma was performed immediately after CT-scan in the first 4 patients and after 2 and 3 months in the last two, as soon as a suspicious thickening of the gastric mucosa appeared evident at CT-scan. All the patients in group A were put under low-molecular weight heparin and subsequently underwent total gastrectomy and lymphadenectomy with a delay of 8 to 13 days from the onset of the

cervical mass and swelling. All the patients in group B underwent radical cervical lymphadenectomy "*en bloc*" with the internal jugular vein first (Figure 2), followed by gastrectomy with lymphadenectomy with a delay of 16 to 96 days. One patient underwent a simultaneous splenectomy for an aneurysm at the hilum of the spleen (7). Once the surgical course was completed, the patients were addressed to the oncology department for an adjuvant treatment and subsequent oncological follow-up. All the patients in both groups received an adjuvant chemotherapy consisting of 5-Fluorouracil and Cisplatin. Further information on the clinical status of the patients and evolution of the disease during follow-up was retrieved from the oncology department. The essential data of patients in group A and B are summarized in Tables I and II.

The primary endpoints of the study were late disease-related survival and rate of cervical recurrence or complications arising from the cervical location of the disease. Postoperative mortality and morbidity were considered as secondary endpoints.

Variables were compared with the Chi square test and survival was expressed with life-table analysis.

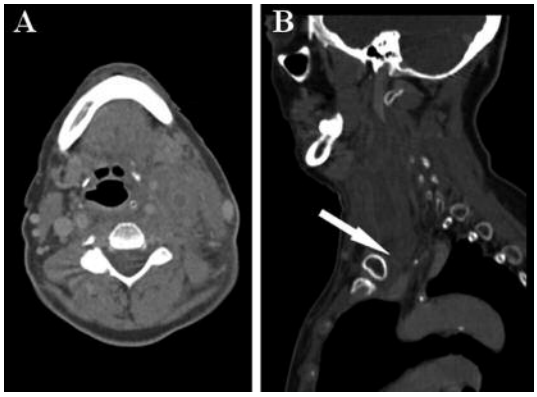

Figure 1. *CT-scan of the cervical region showing thrombosis of the internal jugular vein encased within a confluent lymph nodes' mass (A) and with thrombus extending from below the mastoid process to the jugulo-subclavian venous confluence (B).*

Results

In group B, pathological examination of the resected cervical mass revealed neoplastic proliferation of scarcely differentiated epithelial cells limited to the intraluminal thrombus in the IJV in 4 patients (Figures 3 and 4) without any extension of the neoplasm to the vein wall but with inflammatory involvement of lymph nodes, whereas neoplastic involvement was extended to the vein wall and lymph nodes in 2 patients. These results are summarized in Table III. Pathological examination of the stomach revealed an adenocarcinoma in all the patients.

Primary endpoints. All but one patient in group B, who is alive at 7 months' follow-up, died of disease's progression consisting of distant metastases. The overall patients' survival was 33.3% at 36 months. The mean, group-specific, patients' survival was 15.3 months in group A (range=11-19 months) and 31.2 months in group B (range=7-44 months) (Figure 5) (p=0.11). One patient in group A presented a cervical recurrence of the disease progressing to a distressing dysphagia at 17 months and died of hepatic metastases 2 months later, whereas no patient experienced a cervical recurrence of the disease in group B. One additional patient in group A presented an asymptomatic embolus in the upper lobar division of the left pulmonary artery at 5-month follow-up. Overall, late specific cervical recurrence/complication rate was 67% in group A and none in group B (p=0.02).

Secondary endpoints. Overall, postoperative mortality was absent. One patient in group B (17%), presented a palsy of the facial nerve after resection of the cervical mass. The palsy was completely regressed within 2 weeks. Two patients, one in each group, presented postoperative respiratory complications with a favorable outcome following appropriate medical treatment and support, but this prolonged hospital stay. Overall, postoperative morbidity was 33% in each group (p=1.0).

Discussion

The results of this study indicate that cervical appearance of a cervical mass or swelling due to IJV thrombosis as a paraneoplastic syndrome of Trousseau, associated with gastric cancer, may not necessarily be due to a tumor or necrotic tumor products induced hypercoagulable state alone (3, 8-10) but also to direct seeding of cancer cells migrating through the hematogenous route. In this case, resection of thrombosed IJV and satellite lymph nodes, as a radical neck lymphectomy, may be indicated for more precise diagnosis and staging of the primary gastric tumor and for preventing possible further complications. Such complications include pulmonary embolism and cervical distress due to local progression of the disease despite adjuvant oncological treatment. Based on the present experience with the overall deceiving long term survival of the studied population, the appearance of a cancer-related cervical mass can be considered a sign of dismal prognosis of gastric carcinoma. Cervical resection, therefore, is not focused on prolonging survival but simply on improving the quality of life, despite a light enhancement of transitory postoperative complications compared to anticoagulation and treatment of the primary tumor alone (3-6). Cervical resection may help in the diagnosis of an actually still unknown neoplasm, as macroscopic evidence of the primary tumor may not be evident for 2 to 12 months from the initial presentation of phlebitis-related mass and swelling (11, 12). However, although segmental vein resection in similar cases has been reported in the past (13, 14), and recently with an excellent long-term survival (15), it cannot be proposed as a systematic

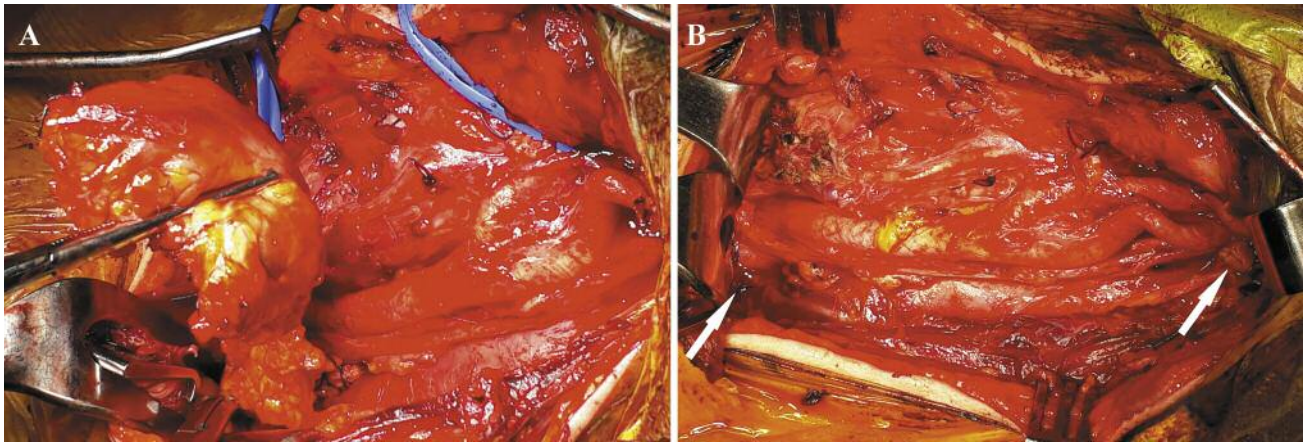

Figure 2. *Intraoperative picture showing progressing, "en bloc" resection of the internal jugular vein and cervical lymph nodes (A) and the completed radical neck dissection: arrows mark proximal and distal ligation of the internal jugular vein (B).*

Table I. *Essential clinical data of patients in Group A.*

Patient (#)	Gender (M, F)	Age (yrs)	Cervical symptoms/signs, distal complications	Post-operative course (Gastrectomy)	Late cervical-related outcomes	Disease-specific survival (months)
1	M	45	Enlarging mass, swelling	Uneventful	Progressing mass, dysphagia	19
2	F	51	Swelling, asymptomatic pulmonary embolism	Postoperative respiratory distress syndrome	Favourable	16
3	M	70	Swelling	Uneventful	Asymptomattic pulmonary embolism	11

Table II. *Essential clinical data of patients on Group B.*

Patient (#)	Gender (M, F)	Age (yrs)	Cervical symptoms/distal complications	Delay neck dissection/ gastrectomy (days)	Post-operative course 1 (cervical)	Post-operative course 2 (gastrectomy)	Late, cervical-related outcome	Disease-specific survival (mths, D/A)
1	M	55	Mass, swelling	73	Uneventful	Uneventful	Favourable	35, D
2	F	72	Mass, swelling	60	Facial palsy	Uneventful	Favourable	7, A
3	F	47	Mass, dysphagia	42	Uneventful	Uneventful	Favourable	41, D
4	M	77	Mass, pain, fever	29	Uneventful	Uneventful	Favourable	38, D
5	M	64	Mass, swelling	35	Uneventful	Respiratory distress	Favourable	22, D
6	M	43	Mass, pulmonary embolism	48	Uneventful	Uneventful	Favourable	44, D

treatment in this setting. In fact, the two patients' groups of this study may not have been perfectly matched, as patients in group A exhibited swelling and mass related to IJV thrombosis alone, whereas in patients in the group B enlarged lymph nodes were more evident, thus suggesting a surgical approach which was not as evident in group A. While a malignant cellular seeding within the lumen of the IJV can only be hypothesized and not demonstrated as they were not operated, it may also be hypothesized that in two patients in group B, presenting undifferentiated epithelial cancer cells both in the thrombus lining the IJV and in the satellite lymph nodes a combination of Trousseau's and Troisier' syndromes may have occurred.

This study has several limitations including its retrospective nature, its long time-span and the small number of included patients. These limitations are partly mitigated by the rarity of the investigated condition, which has been

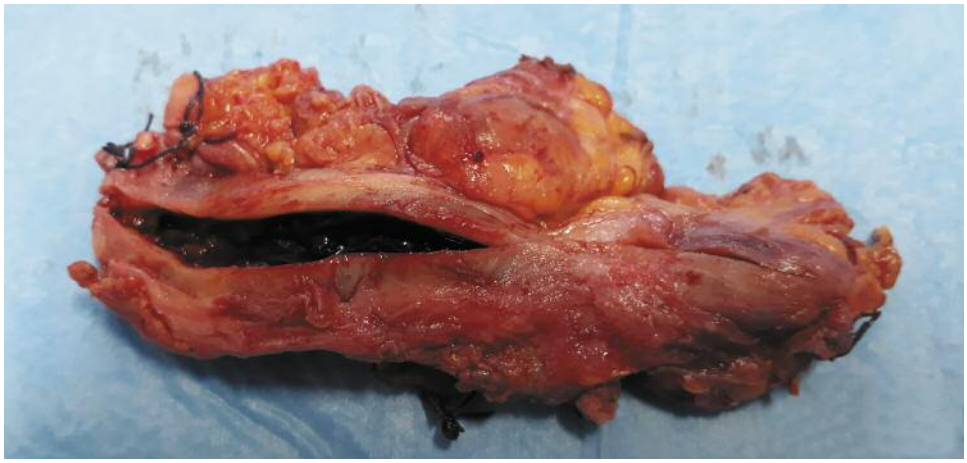

Figure 3. *Resected specimen with intraluminal thrombus in the internal jugular vein.*

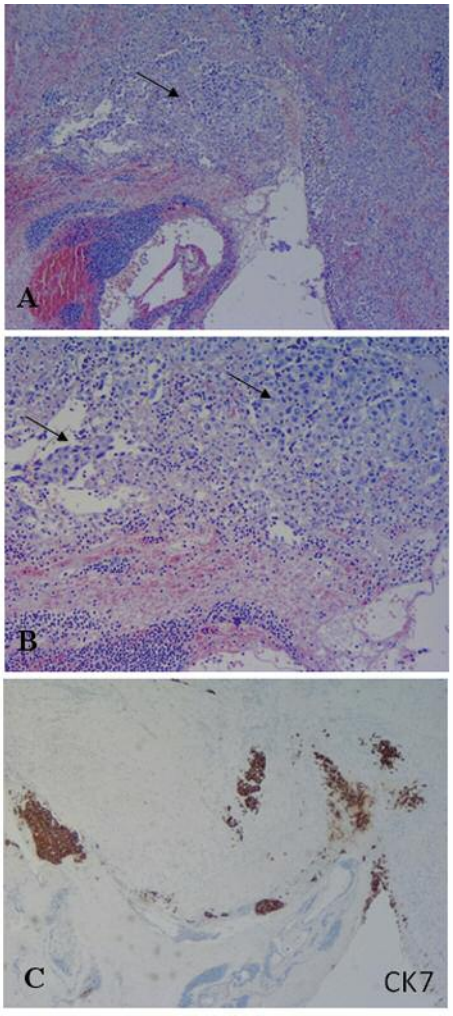

Figure 4. *Pathological examination of the thrombus lining the resected specimen, showing neoplastic epithelial cells within the thrombus (A-B). Cell stain is positive for antibody against cytokeratin 7 (C).*

Table III. *Pathological aspect of resected cervical specimen.*

Patient (#)	Pathology
1	Undifferentiated carcinoma (nodes)
2	Epithelial neoplastic cells (thrombus)
3	Undifferentiated carcinoma (nodes)
4	Epithelial cells (thrombus)
5	Undifferentiated carcinoma (nodes)
6	Epithelial cells (thrombus)

the subject of only isolated case reports so far and by the fact that the data were objectively recorded and reported. Hopefully, this study's preliminary findings will be validated by further larger series.

In conclusion, the results of this study show that "*en bloc*" resection of cervical mass consisting of thrombosed IJV and satellite lymph nodes, due to an asymptomatic primary adenocarcinoma of the stomach may contribute to diagnosis of the primary disease, limit pulmonary embolic complications and improve quality of life by enhancing local control of the disease.

Conflicts of Interest

The Authors declare no conflicts of interest related to this study.

Authors' Contributions

Giulio Illuminati, Antonio Minni, Carla Giordano: Conceptualization; Rocco Pasqua, Priscilla Nardi, Chiara Fratini: Data curation; Giulio Illuminati, Antonio Minni, Carla Giordano: Formal analysis; Rocco Pasqua, Priscilla Nardi, Chiara Fratini: Software; Giulio Illuminati: Supervision; Giulio Illuminati, Antonio Minni, Carla Giordano: Validation; Giulio Illuminati Writing - review & editing; Giulio Illuminati, Rocco Pasqua, Priscilla Nardi, Chiara Fratini, Antonio Minni, Carla Giordano: Final approval.

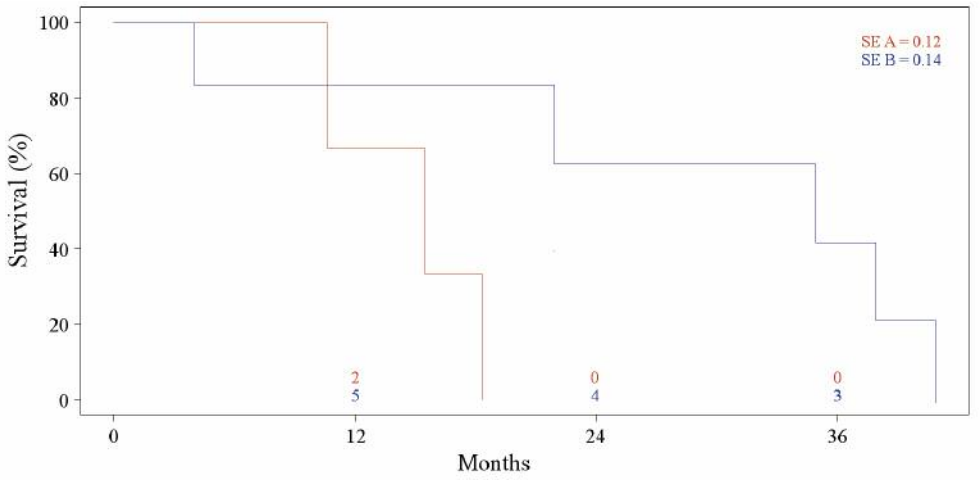

Figure 5. *Kaplan–Meier estimate of survival. Red line, group A; Blue line, group B.*

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