

CASE REPORT

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Detection of Mushroom Extract Use in Patients Coming to the Family Medicine Outpatient Clinic for Routine Check-up and the Relationship Between Changes in Their Clinics

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Abstract

This study focuses on cancer types with high mortality rates, such as stomach and pancreatic cancer, by examining the clinical effects of using the ethyl acetate extract of the lichen species *Usnea longissima*. The study includes a patient with gastric intestinal metaplasia (GIM), a patient with pancreatic cancer, and a patient with stomach cancer.

A 40-year-old woman diagnosed with gastric intestinal metaplasia was positive for *Helicobacter pylori* and had undergone eradication therapy, which she could not complete. She used mushroom extract for 2 months, and a subsequent stomach biopsy showed that intestinal metaplasia was negative.

An 80-year-old woman diagnosed with pancreatic cancer had undergone Whipple surgery and chemotherapy. Afterward, she began using mushroom extract. Imaging reports showed tumor regression, and cancer observed no signs of progression.

A 78-year-old man diagnosed with stomach cancer received six cycles of chemotherapy and used mushroom extract concurrently. Control PET-CT examinations showed a decrease in FDG uptake related to stomach cancer, indicating a positive response to treatment.

Usnea longissima is known for its potent antioxidant effects. This study evaluated the potential anticancer properties of the lichen extract by presenting three patient examples. Notably, the patient with gastric intestinal metaplasia showed improvement after using the mushroom extract despite incomplete *H. pylori* eradication therapy. Similar positive responses to treatment and tumor regression were observed in the pancreatic and stomach cancer cases.

Literature reviews indicate that the anticancer effects of *Usnea longissima* are supported by preclinical studies, but more research is needed for clinical use. Therefore, we believe that the anticancer potential of *Usnea longissima* should be investigated more comprehensively through clinical studies.

Keyword: Gastric intestinal metaplasia, *Usnea longissima*, Ethyl acetate extract

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Stomach cancer is the third leading cause of cancer-related deaths worldwide. The ability to identify early-stage lesions in stomach biopsies has increased interest in developing screening and surveillance strategies to diagnose and prevent stomach cancer early (1).

Gastric Intestinal Metaplasia (GIM) is an early mucosal change with the potential to transform into gastric adenocarcinoma (NCGA). GIM can be easily identified endoscopically and histologically and is an important indicator of stomach cancer risk. Managing modifiable risk factors, such as chronic *Helicobacter pylori* infection, and classifying patients' risks who need endoscopic surveillance play a significant role in reducing stomach cancer mortality (2).

Surgery, chemotherapy, and radiotherapy are commonly used methods in the treatment of stomach cancer. In early-stage stomach cancer, complete tumor removal through surgery is considered the most effective treatment, while in advanced or metastatic cases, chemotherapy

and radiotherapy are used to prolong patients' survival and alleviate symptoms (3).

During follow-up, patients undergo regular endoscopic and radiological evaluations. Especially after surgical intervention, control endoscopies and imaging tests are performed at specific intervals to detect and manage recurrences early. Additionally, evaluating patients' general health status and applying supportive treatments when necessary are important (4).

Pancreatic cancer ranks 14th in incidence but 7th in mortality among global cancers. Due to its aggressive nature, it spreads quickly and has mortal outcomes. Early diagnosis is the most critical factor for effective treatment. Although there is no effective medical treatment for pancreatic cancer, curative treatment may be possible with surgical resection in patients diagnosed early. However, recurrences are also possible (5).

CASE 1

A 40-year-old female patient visited the family medicine outpatient clinic with complaints of a burning sensation in the stomach. The patient reported that the burning sensation in her stomach had been ongoing for the past few weeks, and she had previously experienced similar complaints nine years ago. At the time of admission, the patient's vital

signs were within normal limits. Nine years ago, she had visited an external center with complaints of stomach pain and abdominal cramps, and an endoscopy-colonoscopy was planned. The pathology results from the endoscopic samples showed gastritis and *Helicobacter pylori* positivity. The patient was started on *H. pylori* eradication therapy but could not tolerate the antibiotic treatment and did not complete it. A follow-up endoscopy three years later, in the low-risk group, showed intestinal metaplasia.

There was no other significant medical history besides gastritis and intestinal metaplasia. Her physical examination was normal. The patient's family history included hypertension and diabetes mellitus in her father and hypertension in her mother.

Upon questioning her current medication use, it was discovered that the patient had been using a dietary supplement called mushroom extract for the past two months, which she had obtained from an acquaintance on the recommendation that it was beneficial against cancer. Further investigation revealed that the extract was produced from a lichen called *Usnea longissima*.

The blood tests performed upon her visit were within normal ranges. The patient's full abdominal ultrasound evaluation was normal. She was advised to stop using the mushroom extract and was referred to general surgery for a follow-up. General surgery planned an

endoscopy, and the pathology results of the samples taken showed positive inflammation, negative *H. pylori*, negative intestinal metaplasia, and negative atrophy.

CASE 2

An 80-year-old female patient visited our family medicine clinic to get a prescription for her hypothyroidism medication with no active complaints. Upon reviewing the patient's medical history, it was found that she had presented to the emergency department in July 2021 with abdominal pain, and subsequent examinations revealed gallstones for which she underwent surgery. During her follow-up, a mass was detected in her pancreas via abdominal tomography, diagnosed as pancreatic cancer, and a Whipple procedure was performed. The patient underwent chemotherapy for a year and started using mushroom extract in October 2022.

We examined the imaging reports from the E-nabiz database during her pancreatic cancer follow-up. The upper abdominal contrast-enhanced MR imaging dated 08/10/2021 described: "A nodular mass lesion consistent with liver metastasis, the largest measuring 17 mm in diameter in segment 8, appearing T1 hypointense and T2 hyperintense with heterogeneous enhancement following intravenous contrast material (IVCM). Several contiguous recurrent-residual mass lesions with the largest measuring 48 mm in diameter demonstrating invasion into the portal

confluence at the Whipple operation site. Additionally, a 2.5 cm nodular mass lesion in the tail of the pancreas (recurrent-residual tumor?). Infiltrative soft tissue increments in the mesenteric fat tissue primarily favoring post-operative changes, along with an incision scar line on the anterior abdominal wall related to the previous surgery. Follow-up MR for peritonitis carcinomatosis is recommended."

The abdomen contrast-enhanced MR imaging dated 20/12/2021 described: "A metastatic nodular mass lesion in the liver, the largest measuring 1 cm in diameter in segment 8, appearing T1 hypo, T2 hyperintense with heterogeneous enhancement following IVCN. Several recurrent, residual mass lesions at the portal confluence level, the largest measuring 39 mm in diameter. Compared with the MR examination dated 08.10.2021, findings are evaluated in favor of mild regression with no progression detected."

The abdomen contrast-enhanced MR imaging dated 10/03/2022 described: "A nodular lesion in segment 8 of the liver measuring 8 mm in diameter, appearing T1 hypo, T2 hyperintense with no enhancement following IVCN (inactive metastasis?). Post-operative changes related to the previous Whipple operation and asymmetric soft tissue thickening obliterating the mesenteric fat tissue around the operation site (post-operative fibrotic soft tissue?). Compared with the MR examination dated

20.12.2021, findings are evaluated in favor of regression, with no progression detected."

We noted the regression observed in the abdominal magnetic resonance imaging during the patient's follow-up and the absence of progression.

CASE 3

A 78-year-old male patient visited the family medicine outpatient clinic for routine blood tests. Upon arrival, he had no active complaints. When we inquired about his medical history, we found out that he was diagnosed with stomach cancer in May 2024 and had undergone six cycles of chemotherapy. Additionally, he started using mushroom extract. When we requested the diagnostic tests related to his diagnosis, we were unable to obtain the biopsy result, but there were PET-CT scan results available.

The first PET-CT report dated 19/04/2024 indicated: "FDG uptake consistent with primary malignancy in the stomach (SUVmax: 7.7). Pathological FDG uptake observed in multiple lymph nodes including celiac, gastric, aortocaval, and para-aortic lymph nodes (lymph node metastasis). Suspected invasion in the left lobe of the liver."

The PET-CT report dated 04/09/2024, when compared with the April 2024 PET-CT study, noted: "Nearly complete regression of the previously described stomach uptake, disappearance of the FDG uptake in the lesion

observed in the gastrohepatic area. The lymph nodes observed in the previous study have regressed in number and size, and no FDG uptake was noted. Findings are interpreted in favor of a complete metabolic response to treatment."

In the control PET-CT of our third case, a positive response to treatment was observed.

DISCUSSION

Usnea longissima is a lichen species found in the rain forests of Europe, Asia and North America and is formed by the symbiotic relationship of fungi and algae. It has been used among humans for its antimicrobial, painkiller and antipyretic properties (6).

Usnea longissima extracts have been reported to have strong antioxidant effects. Various free radical scavenging tests revealed that *Usnea longissima* showed excellent reducing power and free radical scavenging capacities in a dose-dependent manner. Sharma and Bhat reported that *Usnea longissima* showed anti-lipid peroxidation effects with scavenging effects on superoxide anion and hydroxyl free radicals. In addition, usnic acid, a metabolite of *Usnea longissima*, has been shown to inhibit inflammation in laboratory and living organisms (6).

It is known that reactive oxygen radicals cause lipid peroxidation (LPO) and produce MDA, the end product of LPO. Odabasoglu et al. reported that usnic acid extract obtained

from *Usnea longissima* showed gastroprotective effect by decreasing LPO and increasing GSH (Glutathione - a powerful antioxidant) levels in ulcers (6).

Antioxidants are substances that, when present in low concentration, significantly reduce the oxidation of the substrate. These antioxidants protect the body from harmful oxidation reactions by reacting with free radicals and other reactive oxygen species. Therefore, free radical-related diseases can be prevented by antioxidant therapy. Recent research has been specifically aimed at finding natural antioxidants of plant origin. Although synthetic antioxidants are currently available, it is thought that some synthetic antioxidants may cause adverse health effects. Therefore, new antioxidants that can be derived from plants are still under investigation. The antioxidant activity of plants is usually due to their phenolic compounds. Flavonoids are polyphenolic compounds with various antioxidant properties. The discovery of antioxidant properties of plants is based on traditional medicine and plants provide a potential source for the development of new drugs (7).

In the study conducted by Mammadov and colleagues in our country, the anticancer effects of the ethyl acetate extract of *Usnea longissima* were investigated in rat models of N-methyl-N-nitrosoguanidine (MNNG)-induced esophagogastric adenocarcinoma. In the study, *Usnea longissima* was administered daily for

six months using oral doses of 50 and 100 mg/kg. The findings showed that the ethyl acetate extract prevented gastric and esophageal cancer and that these doses were non-toxic. Furthermore, no lethal effects were found even at high doses (2000 mg/kg). These results reveal the potential of ethyl acetate extract of *Usnea longissima* to be used in clinical applications in the future (8).

Among the patients we presented in our study, the patient with gastric intestinal metaplasia had interrupted H.Pylori eradication treatment and then used mushroom extract for 2 months and no metaplasia was detected in the control gastric biopsy.

The patient diagnosed with pancreatic cancer received surgical treatment and chemotherapy for her cancer, and the patient diagnosed with gastric cancer received chemotherapy. These two patients received the treatments deemed appropriate by their physicians and started to use mushroom extract as a supplement. Regressions were observed in their follow-up.

The regression in patients diagnosed with gastric cancer and pancreatic cancer with the recovery of the patient with gastric intestinal metaplasia that we have observed suggests that it is primarily due to the effect of medical

treatments, but also suggests that mushroom extract may also contribute to the treatment.

CONCLUSION

When we looked at the literature, it was seen that the investigation of the effect of *Usnea longissima* on cancer was limited to preclinical studies. We think that studies on the effects of *Usnea longissima* should move to the next stage and be tested on humans, and we believe that this may be a promising new treatment option for cancer treatment. Based on the findings of our study, *Usnea longissima* appears to have promising biological activity that warrants further investigation. While our observations are limited to a small number of cases, these preliminary results suggest that this lichen species may have potential for future therapeutic applications. However, larger-scale, controlled studies are needed before any clinical recommendations can be made.

Ethics Committee Approval: Ethics committee approval was received for this study from Non-Interventional Scientific Clinical Research Ethics Committee of Ordu University. (Date: 07.03.2025 and number: 78). The study was carried out by paying attention to the Declaration of Helsinki.

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Interpretation: OE, MKO, BCA, HS, Writing: OE, MKO, BCA, HS

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