Review of a non-epithelial tumour of the small bowel after c-kit revolution

Ann. Ital. Chir., 2015 86: 183-185
pii: S0003469X16024362

Enrico Fiori, Daniele Ferraro, Alessandro De Cesare, Giovanni Leone, Cecilia Barmann, Alberto Schillaci, Francesco Borrini

Department of Surgery "Pietro Valdoni", "Sapienza" University of Rome, Rome, Italy

Review of a non-epithelial tumour of the small bowel after c-kit revolution

In this article, we reviewed the case of a patient who was object, in 1999, of a published case report of schwannoma of the jejunal wall. Recently, the patient has been referred to our institution for a mass of the stomach identified by upper gastrointestinal endoscopy. The patient underwent a wedge resection of the stomach and a histopathological diagnosis of GIST of the stomach, based on a positive immunohistochemical staining of c-kit and CD34, was made. In consideration of these findings, we performed immunohistochemistry for c-kit and for CD34 on the previous lesion of the jejunal wall, which resulted strongly positive for CD117 and negative for CD34. A new diagnosis of gastrointestinal stromal tumour (GIST) of jejunal wall with moderate risk of progression was made. The lesion was also classified, according to the AJCC Seventh Edition, as a pT3, pN0, Stage II, GIST. This case shows the importance of a reassessment of the diagnosis of mesenchymal neoplasm of the small intestine made before the development of anti-CD117 antibody for a correct prognostic stratification, a better therapeutic management and a close follow-up, if necessary.

KEY WORDS: Adjuvant therapy, c-kit, GIST Imatinib

Introduction

A variety of mesenchymal neoplasm may arise from the gastro-intestinal tract and the most frequently identified are leiomyomas and schwannomas, being neurofibromas and ganglioneuromas more rare [2,3]. GIST represents less than 1% of the malignancies of the gastro-intestinal tract (4). Before the advent of C-kit revolution, differential diagnosis between those neoplasm and gastrointestinal stromal tumour (GIST) was undoubtedly difficult and often missed.

C-kit, also known as CD117, is a tyrosine kinase receptor of the immunoglobulin supergene family. This antigen is widely expressed in haematopoietic stem cells, mast cells, melanocytes, various ductal epithelia and elsewhere. Expression is also characteristic of the gut pacemaker cell, the interstitial cell of Cajal [5]. It is now eviden that between 68% and 90% of GISTs shows strong expression for c-kit, together with the expression of CD34, and a gain-of-function mutation in the c-kit gene appears to be a novel and specific feature of GISTs. C-kit (CD117) is undoubtedly a diagnostically useful immunohistochemical marker and its mutation appears to have important prognostic implications [6]. Recently, other markers with high diagnostic specificity for GIST have been identified: DOG1 (Discovered on GIST 1), expressed in 98% of GIST, and PKCq (isoform of PKC family) [7].

Pervenuto in Redazione Luglio 2015. Accettato per la pubblicazione Settembre 2015
Correspondence to: Prof. Enrico Fiori, Via Città della Pieve 88, 00191 Rome, Italy (e-mail: enrico.fiori@uniroma1.it)

The widespread of tests evaluating c-kit expression by GIST cells will solve diagnostic problems with other mesenchymal neoplasms. In fact, other mesenchymal neoplasms of the gastro-intestinal tract, such as those originating from smooth muscle cells or from interstitial cells of Cajal, are frequently negative for the expression of CD117 at immunohistochemical evaluation [5].

Case Report

A 67-year-old male, already operated in our Surgical Department in 1999 for a schwannoma of the jejunal wall, referred to our institution for a gastric mass detected during an endoscopic examination. The patient was completely asintomatic. Esophagogastroduodenoscopy showed a submucosal mass in the posterior wall of the gastric body. An endoscopically-taken biopsy only revealed signs of mild gastritis. Computed tomography of the abdomen was performed and it revealed a 10-mm protruding mass at the posterior wall in the upper body of the stomach. No other masses were found. Routine laboratory parameters and the concentration of CA 72.4 were found to be normal. Under general anesthesia, the patient underwent an open wedge resection of the stomach based on the preoperative suspicious of GIST.

Macroscopically, the resected tumour was well circumscribed and measured 12 mm, without signs of ulceration. The cut surface of the tumour appeared yellowish-white and solid. The histopathology showed that the tumour was located mainly in the proper muscle layer of the stomach and consisted of spindle cells (Fig. 1). mitosis nor necrosis were found.

Immunohistochemical staining of c-kit and CD34 were positive (Fig. 2-3). Moreover the tumour was immunohistochemically negative for S-100 protein and SMA. The diagnosis of gastrointestinal stromal tumour (GIST) of the stomach was posed and it was classified, according to the AJCC, as a pT1, pNX, pMX, Stage IA GIST of the stomach.

We decided to review the old jejunal mass. In the 1999 we had produced a diagnosis of schwannoma of the jejunal wall. The tumour was positive for vimentin and S100 protein, negative for muscle-specific-actin, desmin, and NSE. We have assessed the lesion for c-kit and CD34 and it resulted to be strongly positive for CD117 and negative for CD34. In consideration of monomorphic aspect of cellular population, scanty mitosis (up to two mitosis per 50 HPF), maximum size measuring smaller than 7 cm, we modified the diagnosis on the basis of new parameters [8]. Then, the new diagnosis was a gastrointestinal stromal tumor (GIST) of jejunal wall with moderate risk of progression. The lesion was also classified with AJCC Seventh Edition as a pT3, pN0, pMX, Stage II GIST of the jejunal wall. The patient was investigated for others systemic and familial diseases. The

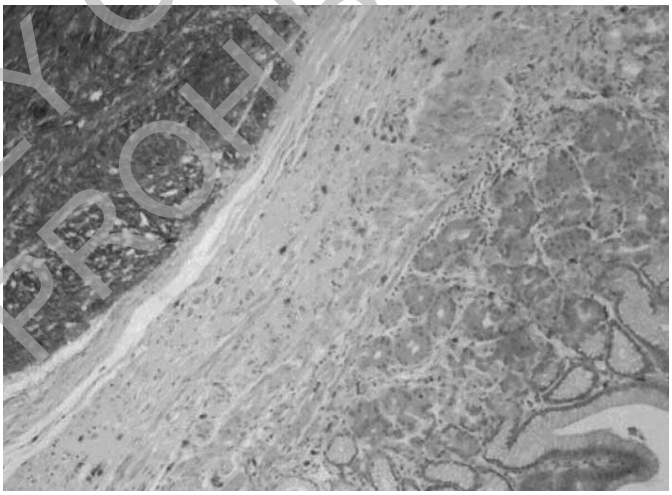

Fig. 2

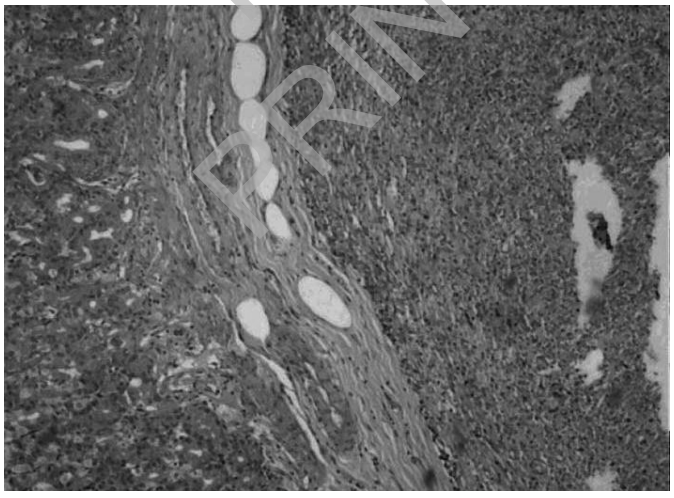

Fig. 1

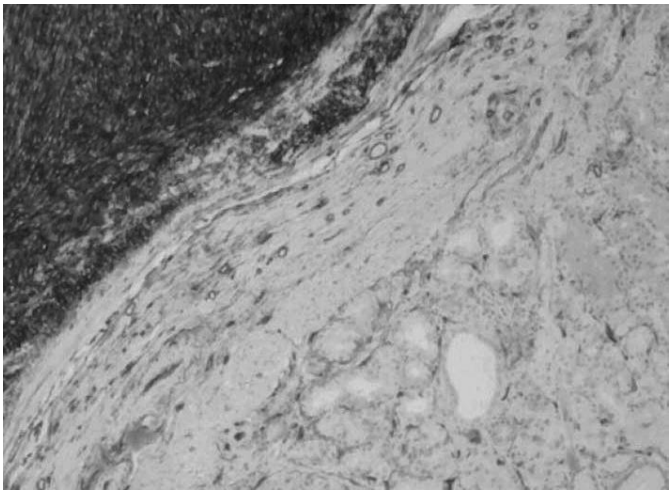

Fig. 3

familiar anamnesis and the clinical examination were negative for other pathological associations. Six months after surgery, there's no evidence of recurrent disease or metastases.

Discussion

Today c-kit (CD117) is undoubtedly a diagnostically useful immunohistochemical marker and its mutations appear to have important prognostic implications [8]. Until the development of anti-CD117 antibody, it was impossible to make a correct diagnosis of gastrointestinal stromal tumor (GIST) and so we produced a diagnosis of schwannoma of the jejunal wall. That is the reason why most of the mesenchimal lesions of the gastrointestinal tract identified before the advent of the c-kit revolution should be evaluated again and properly classified. Moreover, according to the current GIST prognostic classification, tumours previously considered benign could have a moderate to severe grade of recurrence risk and so they could deserve a stricter follow-up. In absence of an optimal codified surgical procedure, the limited surgical resection with clear margins, when feasible, gives an excellent disease free survival, in accordance to other authors [9,10]; this patient has a 24% chance of recurrence, which is considered intermediate; the question that arises is, should this patient be treated with adjuvant therapy with Imatinib? This question underlines the necessity of a validate stratification system with the introduction of new variables such as tumour rupture, necrosis, and genotype, to increase the accuracy of predicting disease free survival and to improve the treatment outcomes [11].

Conclusion

The purpose of this article is to enhance the role of c-kit in the correct classification of all non-epithelial tumours of the gastro-intestinal tract. The reassessment of diagnosis of mesenchimal lesions made before the advent of the immunohistochemical assay for c-kit is important for a correct prognostic evaluation in order to eventually submit the patient to adjuvant therapy with imatinib and to set up an adequate follow-up.

Riassunto

L'articolo proposto descrive un caso clinico di GIST della parete gastrica in un paziente già sottoposto nel 1999 a resezione intestinale per neoformazione mesenchimale del digiuno. Gli autori pongono l'attenzione sulla necessità di rivalutare immunoistochimicamente le lesioni mesenchimali diagnosticate prima dell'avvento di c-kit al fine di ottenere un migliore inquadramento diagnostico e prognostico. Infatti, la diagnosi differenziale tra GIST e le altre neoplasie mesenchimali del tratto gastro-intestinale, quali leiomiomi, schwannomi, neurofibromi e ganglineuromi, era praticamente impossibile prima dell'avvento del c-kit. Identificare i GIST tra quelle che un tempo venivano classificate come neoplasie mesenchimali consentirebbe di offrire ai pazienti la possibilità di beneficiare, qualora fosse indicato, del trattamento neoadiuvante con Imatinib o, alternativamente, di più stretti schemi di follow-up al fine di diagnosticare in maniera precoce eventuali recidive di malattia.

References

1. Fiori E, Mingazzini PL, Lutzu ES, et al.: *Small bowel schwannoma with diffuse subcutaneous lipomatosis. Case report and literature review*. Ital J Gastroenterol Hepatol, 1999; 31:868-71.

2. Bononi M, De Cesare A, Stella MC, Fiori E, Galati G, Atella F, Angelini M, Cimitan A, Lemos A, Cangemi V: *Isolated intestinal neurofibromatosis of the colon. Single case report and review of the literature*. Dig Liver Dis, 2000; 32:737-42.

3. Fiori E, Pozzessere C, Lamazza A, Leone G, Borrini F, Schillaci A, Mingazzini P: *Endoscopic treatment of ganglioneuroma of the colon associated with a lipoma: A case report.* J Med Case Reports, 2012; 14; 6(1):304.

4. Sianesi M, Bezer L: *GIST: una patologia in continua evoluzione. Strategie diagnostico-terapeutiche.* Ann Ital Chir, 2009; 80:257-60.

5. Pericoli Ridolfini M, Cassano A, Ricci R, Rotondi F, Berardi S, Cusumano G, Pacelli F, Doglietto GB: *Tumori stromali gastrointestinali*. Ann Ital Chir, 2011; 82:97-109.

6. Morson and Dawson's. Gastrointestinal Pathology. Fourth Edition. London: Blackwell Publishing; Chapter 15.

7. Ferrocci G, Rossi C, Bolzon S, Della Chiesa L, Tartarini D, Zanzi F, Durante E, Azzena G: *Gastrointestinal stromal tumours. Our experience ten years later*. Ann Ital Chir, 2011; 82:267-72.

8. Miettinem M: Semin Diagn Pathol, 2006; 23:70-83.

9. Buchs NC, Bucher P, Gervaz, et al.: *Segmental duodenectomy for gastrointestinal stromal tumor of duodenum*. World J Gastroenterol, 2010; 16(22): 2788-792.

10. Chung JC, Chu CW, Cho GS, et al.: *Management and outcome of gastrointestinal stromal tumor of the duodenum.* J Gastrointest Surg, 2010; 14:880-83.

11. Shreyaskumar Patel, MD: *Navigating Risk Stratification Systems for the Management of Patients With GIST*. Ann Surg Oncol, 2011; 18:1698-704.