# Gardner-Diamond syndrome: Difficulties in the management of patients with unexplained medical symptoms

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The case of an adolescent girl who presented with unexplained bruising is reported. Subsequent investigations failed to elucidate an organic etiology. The diagnosis of Gardner-Diamond syndrome – a syndrome of predictable bruising preceded by pain and warmth at the bruise site, often associated with physical or psychosocial stress – was made. In the present report, the authors use their experience with this rare syndrome to highlight some important ethical and practical considerations with regard to investigation, treatment and communication in illnesses with unexplained medical symptoms.

**Key Words:** *Gardner-Diamond syndrome; Unexplained medical symptoms*

## Le syndrome de Gardner-Diamond : Les problèmes de prise en charge de patients ayant des symptômes médicaux inexpliqués

Le cas d'une adolescente qui a consulté à cause d'ecchymoses inexpliquées est présenté. Tous les examens exécutés pour établir une étiologie organique étaient normaux. On a posé un diagnostic de syndrome de Gardner-Diamond, un syndrome d'ecchymoses prévisibles précédées par des douleurs et une sensation de chaleur au foyer de l'ecchymose, souvent associé à un stress physique ou psychosocial. Dans le présent article, les auteurs se servent de leur expérience de ce syndrome rare pour souligner quelques considérations importantes au point de vue éthique et pratique, en ce qui a trait aux examens à effectuer, au traitement à amorcer et aux communications dans le cadre d'une maladie aux symptômes médicaux inexpliqués.

Illnesses in which psychosocial issues play a major role in the onset and/or maintenance of symptoms can be difficult to manage in the medical setting. Physicians in general have difficulty dealing with ambiguity and uncertainty. This situation can occur when there are unexplained medical symptoms. There is always pressure to perform specific tests to establish a diagnosis that has a clear etiology, explains the symptoms, and can be treated easily. When this is not possible, as in the situation where psychosocial issues play a major role in the onset and maintenance of symptoms, the medical team, as well as the patient and family, can become frustrated. This can lead to difficulties in communication.

It is important that the medical team have an organized approach to the investigation and treatment of disorders in which psychosocial factors may play a major role (1,2). Once the diagnosis is made, a clear plan needs to be established by the medical team, and open communication with the patient and family is essential to maintain rapport and ensure a successful outcome.

There are many examples of unexplained medical symptoms, such as recurrent abdominal pain of childhood and headaches – often described as 'the diagnosis of exclusion'. The present report describes a case of Gardner-Diamond syndrome and highlights some of the difficulties encountered when this rare syndrome presents in the medical setting. Because this syndrome is rare, it was not initially considered in the differential diagnosis of the present case. It thus became truly a 'diagnosis of exclusion', added to the list of differential diagnoses when investigative options were exhausted. This forced us to explore more carefully how to communicate findings, proceed with therapy, and eventually halt investigations in a syndrome where symptoms simply cannot be explained. Although this is a more unusual example of a condition with unexplained medical symptoms, the principles are applicable to more common conditions.

## CASE PRESENTATION

An adolescent girl presented with a one-day history of right lower quadrant abdominal pain radiating to the right flank and back that was associated with nausea and vomiting. A similar episode of abdominal pain occurred one year earlier and was attributed to a ruptured ovarian cyst. On physical examination, a 5 cm × 5 cm bruise was present over her right lower quadrant, the area of maximal abdominal tenderness. Initially, the surgery team was involved with her care. They excluded a surgical etiology with the assistance of several radiological investigations (abdominal radiographs, abdominal and pelvic ultrasounds, a computed tomography scan of the abdomen, and upper gastrointestinal series with small bowel follow-through), all of which were normal. She was transferred to the paediatric medicine service for further evaluation and management.

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There was no history of trauma or prodromal symptoms. She did not have a history of abnormal bleeding or easy bruising. There was no menorrhagia, hematuria or dysuria. Recent wisdom teeth extraction was not complicated by excessive bleeding. Oral contraceptives had been discontinued two months before admission. At the time of admission, the patient was not taking any medications or herbal remedies. Her family history was unremarkable for bleeding disorders. With respect to social history, the patient's father had recently died of a chronic illness. Both the patient and her mother were familiar with the health care system.

Over the next several days, more bruises developed. The bruises followed a symmetric pattern, with subsequent bruising occurring on the right and left posterior flanks, and the left lower quadrant. Bruises then appeared on her right and left anterior thorax, below her clavicles. Interestingly, the patient was able to predict the appearance of her bruises. She described a sensation of pain and warmth deep under the skin at a particular site, and within 24 h a bruise would develop there. In this way, the patient predicted almost exactly where subsequent bruising would occur. On examination, the bruises were similar in size (usually 5 cm to 8 cm in diameter), tender to palpation, not palpable, present for approximately 10 days, and limited to the trunk. Nonaccidental trauma, Munchausen's syndrome and Munchausen by proxy were considered and ruled out after careful questioning and observation.

Bloodwork was done in a stepwise fashion, with normal results prompting further investigations. Initial bloodwork, including complete blood count, international normalized ratio, partial thromboplastin time, fibrinogen and liver function tests were normal. This was followed by platelet aggregation studies, von Willebrand factor, protein C and S, and antithrombin III, which were normal. Rheumatological investigations, including erythrocyte sedimentation rate, rheumatoid factor, C-reactive protein, lupus anticoagulant, anti-double-stranded DNA and perinuclear antineutrophil cytoplasmic antibodies were normal. Porphyrin screen was negative. Complement and immunoglobulin levels, and protein electrophoresis were normal. Viral studies, including tests for hepatitis B and C, cytomegalovirus and Epstein-Barr virus, were negative or indicative of either past exposure or previous immunization. A skin biopsy of the bruise showed nonspecific lymphocytic infiltration and hemorrhage. There was no evidence of vasculitis, and immunofluorescence studies were negative. An upper endoscopy demonstrated esophagitis, but was otherwise normal. Consultation with several specialists (hematology, rheumatology and gastroenterology) at the Children's Hospital of Western Ontario (London, Ontario) and other regional tertiary care centres failed to identify an organic etiology.

As the bruises developed, the patient continued to complain of abdominal pain and nausea. She also developed emesis and lost her appetite. One week after admission, she developed headaches; a cranial computed tomography scan was normal, specifically showing no evidence of an intracranial bleed or other space-occupying lesions. Her ongoing pain required narcotics, which were delivered by patient-controlled analgesia because oral and intravenous analgesia administered as needed failed to control her symptoms. Poor oral intake with nausea and vomiting necessitated the use of total parenteral nutrition, requiring frequent intravenous line changes. Both the patient and her family were becoming increasingly concerned with her ongoing symptoms and the lack of a diagnosis.

Gardner-Diamond syndrome was considered to be the most likely diagnosis. This diagnosis was made based on the patient's symptoms of predictable bruising, nausea and headache associated with psychological stress, and the lack of evidence for hematological, vascular, immunological or infectious abnormalities. This information was presented to the patient and her mother and was met with strong resistance. They refused psychiatric evaluation. Intravenous nutrition and analgesia were gradually reduced and then discontinued. The patient's pain gradually subsided, her headaches resolved, oral intake improved and there was no new bruising. She was discharged 23 days after admission on omeprazole, an oral laxative, and acetaminophen with codeine as needed. Outpatient follow-up with a community paediatrician was arranged. Within 10 days of discharge, the bruises had resolved significantly, and several months later the patient had recovered completely.

## DISCUSSION

### Gardner-Diamond syndrome

Gardner-Diamond syndrome (3-8), also known as autoerythrocyte sensitization or psychogenic purpura, is a rare clinical syndrome of recurrent bruising or bleeding, usually following a physical or psychosocial stress. It most commonly affects women and has been described in children and adolescents (5,7). Bruises can develop anywhere on the body but are usually located on the extremities. There is usually a prodrome of warmth and pain at the bruising site, or systemic symptoms such as headache, nausea or vomiting. Organic factors are seldom identified. Skin biopsy shows extravasated red blood cells but no evidence of vasculitis.

This illness represents a type of chronic unexplained medical symptom where patients present with real, sometimes bewildering, medical signs and symptoms. Often times, psychiatric symptoms are not initially explored. A search for an organic etiology to explain the problem is initiated, but is usually not fruitful. Symptoms are treated medically, with variable results. A careful history regarding emotional and social stress is often not elicited until all medical tests and treatments have been exhausted. This leaves the medical team and the patient and family frustrated. The patient's frustration may be exacerbated by the suggestion that the illness is influenced by psychosocial issues. Communication becomes difficult and dilemmas arise around the utility of further testing and continuation of

medical treatment. In the end, the experience is often unsatisfying for both the patient and the medical team.

In the present report, we discuss issues specific to this case. These issues can be generalized to other illnesses in children and adolescents, which include unexplained medical symptoms associated with psychosocial factors.

**The investigation and medical treatment of unexplained medical symptoms**

A hypothesis to explain the symptoms of Gardner-Diamond syndrome is autosensitization to the patient's own erythrocytes. This hypothesis led to the development of a test that involves the subcutaneous injection of the patient's own blood and a control injection (eg, plasma or normal saline). Subsequent bruising at the site of injection of the patient's own blood is presumed to support the diagnosis of autoerythrocyte sensitization. The hypothesis of autoerythrocyte sensitization was originally proposed by Gardner and Diamond (6), who described the first four cases in 1955. However, this theory has never been proven, and the usefulness of the test itself remains controversial. Investigators have reported positive responses to numerous injected agents and control substances (eg, normal saline). Many negative responses have also been reported (3). In a case series by Ratnoff (3), only 35 of 59 tests produced a positive response to the injection of whole blood. Ratnoff even proposed that the test is affected by the patient's awareness of doubt in the investigator's mind as to whether the test is really useful. In fact, Ratnoff often omits the procedure. To date, there is no definitive laboratory test to diagnose Gardner-Diamond syndrome. The diagnosis is therefore made based on the patient's history and physical examination, and through exclusion.

In the present case, the patient's reluctance to accept the diagnosis made us question the usefulness of the test described above, especially since its validity is potentially dependent on the expectations of the patient. If we tested her and the result was negative or equivocal, then it would have been difficult for us to convince her that she had Gardner-Diamond syndrome. A positive result would have led the patient to question the validity of the test. Furthermore, we wondered how one interprets a test of unknown specificity and sensitivity. We were also uncertain whether we could properly administer the test. In general, a test should be performed if it will add new information. We did not believe it would, having ruled out all other causes.

Having established the diagnosis, we became increasingly concerned about the effects of both further tests and the current treatment we were offering. Although our treatment could be described as 'symptomatic' or 'supportive' (total parenteral nutrition, narcotic analgesia), these treatments are not without side effects themselves. Narcotic analgesia needs to be closely monitored (a dosing error occurred on one occasion), and total parenteral nutrition can be harmful to the liver, often requiring prolonged intravenous access. The patient's mother asked us whether a central line should be inserted. It became apparent that our goal to 'do no harm' was being cast into doubt. With confidence in the diagnosis of Gardner-Diamond syndrome, the risks of further testing and medical therapy were deemed to outweigh the benefits. Medical treatment was gradually, and successfully, diminished. This, coupled with reassurance to the patient and her family that we were confident in our diagnosis, led to a gradual cessation of symptoms and eventual discharge from hospital.

In situations where medical symptoms are deemed 'unexplained', it may sometimes be useful to offer a physiological hypothesis of why these symptoms may be occurring, even when the psychosocial aspect is obvious from the beginning. Admitting to the patient that many aspects of how the brain and body interact remain unknown could help the patient accept that psychosocial factors may play a role. Explaining to patients that the symptoms they are experiencing are real (which they are) gives legitimacy to their concerns and helps them feel that their complaints are being listened to. Sometimes, even offering a 'possible medical explanation' from the list of differential diagnoses (for example, an ' atypical viral syndrome' or 'atypical purpuric syndrome'), as well as offering medical advice that seems reasonable for this explanation (for example 'drink lots of fluids and slowly resume normal activities'), allows patients to accept the medical opinion without having to admit to the psychosocial overlay. The psychosocial factors can then be explored later. However, if it becomes apparent that a patient will demand more investigations or potentially harmful treatment, then it may be necessary to be firm and state that further medical intervention will not be helpful.

It can be difficult to say 'no' to ongoing investigations and treatment, but this is justified when the therapy is considered "bad medicine and against accepted medical practice" (2). For this reason, it may be important to consult other services or specialists within the institution or, if necessary, at another institution.

**Communication issues**

The underlying psychological stress often accompanying Gardner-Diamond syndrome was subtle in our patient. There were no overt signs of depression, anxiety or psychosis. There had been major stressors in her life before this illness, which were related primarily to the family dynamics and the recent death of her father. However, these stressors were explored later in the management of this syndrome (as rapport was established) and were overshadowed by the search for an organic etiology. Campbell et al (5) noted that "the patients at first glance appear to be quiet, shy, pleasant, and seemingly well-adjusted, but on careful probing are often found to have extremely abnormal backgrounds". This description fits our case in some respects. Unfortunately, the literature abounds with cases describing an association between this disorder and major psychiatric symptoms. The patient and her family's awareness of this fact resulted in their reluctance to accept the diagnosis and made the patient-physician interaction challenging. Initially, the rapport between the patient and the

health care team was good, and there was a perception by the patient and her family that all of the appropriate tests were being ordered and that potential etiologies were systematically being ruled out. However, when the possibility of Gardner-Diamond syndrome was raised, there was strong resistance by the patient and her family to accept this diagnosis. This was due to their reluctance to accept psychosocial factors as playing a significant role in the development of this disorder. The importance of careful communication was underscored. We specifically decided to avoid using the term 'psychogenic purpura'. We also avoided naming the disorder 'autoerythrocyte sensitization' because it suggests an organic disorder. For this reason, we believe the eponym 'Gardner-Diamond syndrome' is the best name to communicate to the family. It avoids the immediate stigmatization imposed by the term 'psychogenic purpura'.

Disclosure of the diagnosis of illness in which psychosocial factors play a significant role can be very difficult. The medical team has three options. The first option (the one we chose initially) includes recommending a full biopsychosocial evaluation while discontinuing further tests and nonessential treatment. A second option involves fabricating a medical diagnosis, withholding the true diagnosis and then suggesting a medical approach to resolve the illness. This may be tempting in difficult situations, but would be unethical and dishonest. In the long term, withholding information usually results in negative repercussions. The third approach is a more gradual approach and involves offering physiological discussions of the illness, gradually easing medical therapy, and limiting tests (especially those that are costly or invasive), while suggesting that there is a psychosocial component to this illness that warrants further investigation. Because our patient refused a full biopsychosocial evaluation, the third approach was eventually used and accepted by both the patient and her mother.

It is appropriate for the physician to express their opinion rather than simply putting forward the technical details and then offering to do whatever the patient wants. Patients usually respect the clinical judgment of the physician, and this is usually well received when good rapport has been established (1).

Finally, especially in situations where adolescent patients are involved, it is important to listen to what the patient is saying, apart from the family. Listening to them and giving them a role in the health care decision-making process is vital (2).

## CONCLUSION

The present case describes the rare disorder of Gardner-Diamond syndrome in an adolescent. It highlights a number of issues relevant to this diagnosis and the diagnosis of other disorders where there are unexplained medical symptoms in which psychosocial factors play a significant role. Proper communication and confidence in the diagnosis of these illnesses, once established, is important and will reduce the risk of over-investigation and over-treatment and enhance continuing rapport between the patient and the medical team.

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