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Case Report: Dropsy Outbreak in a Single Family in Punjab, India

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Abstract. Epidemic dropsy is caused by consumption of mustard oil contaminated with argemone oil. It usually occurs in outbreaks with acute manifestation of bilateral pitting edema, erythema, and local tenderness along with cardiac and respiratory problems in severe cases leading to death. We report an outbreak that is unusual because of its gradual onset, clustering in a single family, and with major manifestation of gastrointestinal illness mimicking acute gastroenteritis, hence leading to delayed diagnosis and high mortality. Thus, the diagnosis of epidemic dropsy should be considered as a strong possibility when there is clustering of cases in a single family with on and off gastrointestinal symptoms of vomiting and diarrhea in a mustard oil consuming belt.

INTRODUCTION

Many outbreaks of dropsy have been reported from India since 1877, when the first case was reported.[1] Epidemic dropsy results from ingestion of edible oil adulterated with *Argemone mexicana* (Mexican poppy) oil.[2] It is an acute noninfectious disease characterized by pitting edema of the extremities, especially of the lower limbs; cutaneous erythema; and local tenderness.[3,4] Glaucoma and other visual field defects, leading to blindness, and cardiac and respiratory problems, leading to death are among the most severe manifestations of the condition.[5–9]

The outbreaks of dropsy have their maximum episodes during the summer months of July–August in India because newly extracted oil harvested from agricultural produce is sold during these months in the market.[10] In the month of August 2011, the Civil Surgeon of the district Shahid Bhagat Singh Nagar (SBS Nagar), Punjab informed the District Surveillance Officer (DSO) that there was a suspected outbreak of epidemic dropsy in a single family at village Fatehgarh in the district. The DSO immediately informed the State Nodal Officer, Integrated Disease Surveillance Project (IDSP), Punjab and constituted a rapid response team to investigate the disease. The School of Public Health, Post-Graduate Institute of Medical Education and Research (PGIMER), Chandigarh was contacted to provide technical and laboratory support for the outbreak investigation. In this work, we present the unusual presentation of epidemic dropsy leading to delayed diagnosis and treatment.

MATERIAL AND METHODS

The investigations were carried out by the rapid response team led by the DSO to determine the cause of outbreak. All members of the concerned family were interviewed and those requiring medical attention were hospitalized. A survey of the surrounding area was conducted to identify similar cases in the vicinity, if any. A thorough personal and medical history, history of present illness, and clinical features of each patient was noted. Blood was collected for hemoglobin, total leukocyte, and differential leukocyte counts and urine samples were collected for urine examination and sanguinarine detection from all the patients and sent to the School of Public Health for analysis. The same were later forwarded to the National Institute for Pharmaceutical Education and Research (NIPER) at Sahibzada Ajit Singh Nagar (SAS Nagar) District, Punjab for bio-chemical investigations. Follow-up of the patients was again done after 1 year to check for the residual signs and symptoms by a team from PGIMER. Written informed consent before data collection was obtained from all the study participants and ethical clearance was obtained from the Institutional Ethics Committee for this study.

Mustard oil samples were collected from the affected family, six neighboring households, and from the shop where the family got mustard oil extraction done. The oil samples were tested for contamination of argemone oil using the ferric chloride test and later confirmed by thin layer chromatography (TLC) under UV light. The oil samples were analyzed by Public Analyst at State Food, Drugs & Excise Laboratory, Punjab. The ferric chloride method required dissolution of 5 mL oil into 5 mL of toluene solvent, to which the same amount of concentrated hydrochloric acid was added. The acid layer formed was then separated and moved into another test tube, to which 1 mL of ferric chloride solution was added. The test tube was heated in a boiling water bath for 10 minutes and observed for the presence of needle-shaped brown crystals.

For the thin layer chromatography technique, 5 mL of oil was dissolved in 5 mL diethyl-ether to which 5 mL of concentrated hydrochloric acid was added. The mixture was first shook and then heated in a hot water bath for about 10 minutes. The acid layer that formed was transferred to another beaker and heated in a boiling water bath; the contents evaporated leaving behind the dry residue. The residue thus obtained was dissolved in 1 mL of chloroform and acetic acid mixture and spotted on a TLC plate with the help of spotting capillary. The plate was then developed in butanol, acetic acid, and water mixture, and the solvent front was allowed to move up to a distance of 10 cm, which was then checked for presence of fluorescent spot under UV light.

Serum samples of all the living patients were also collected and examined for presence of sanguinarine. These tests were carried out using the high-performance liquid chromatography method at the department of Pharmacology and Toxicology, NIPER, SAS Nagar, Punjab. The procedure suggested by Hoellinger and others in their work published in 2003 was

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followed.[11] For extraction of the samples, 10 μL of formic acid was added to 1 mL of plasma sample to adjust the pH between 3 and 3.5. After vortexing the sample was evaporated under a nitrogen stream. Dry residues were dissolved in 250 μL of water and added to 5 mL of the mixture water/acetonitrile 50/50 (v/v) with 0.2% formic acid. The resulting mixture was shaken for 10 minutes and centrifuged for 20 minutes at 6,000 × *g* to discard denatured proteins. The supernatant was removed and evaporated under nitrogen to an extent as much as was possible, and was finally reconstituted in 200 μL of water/acetonitrile 80/20 (v/v) with 0.2% formic acid. The sample was injected onto a C18 column, running at room temperature with a flow rate set at 1 mL per minute. Eluent A consisted of water/acetonitrile 80/20 (v/v) with 0.2% formic acid and eluent B was water/acetonitrile 5/95 with 0.2% formic acid. A 15-minute linear gradient was started from 100% of eluent A to 100% of eluent B and was then followed by 100% eluent B for 5 minutes. Sanguinarine was monitored with UV detection at 327 nm. A linear curve was fitted after monitoring of UV detection of sanguinarine standards at various concentrations (10, 25, 50, 75, and 100 μg/mL). The correlation coefficients calculated from UV monitoring of calibration curves of sanguinarine ($r^2 = 0.999$) attested the linearity of the detection. The levels of the unknown samples were read from the standard curve and expressed as μg/mL.

RESULTS

A total of 10 persons were affected during the outbreak, of which four were children. There were two deaths during the outbreak (case fatality ratio: 20%). All the patients belonged to a single joint family. None of the persons living in the neighboring households complained of similar illness. The family belonged to a lower middle class, and the main occupation of the family was agriculture. The age of the patients ranged from 2 to 60 years of age.

There was an insidious onset of signs and symptoms. All of them initially presented with intermittent episodes of diarrhea and vomiting over a period of 1–2 months. The initial symptoms were misinterpreted to be caused by acute gastroenteritis and were provided with symptomatic treatment. Five of the patients were admitted and discharged from various hospitals at different times from June 2011 to August 2011. The possibility of dropsy was considered only after 4–6 weeks, when the patients had presented with severe symptoms such as breathlessness and pitting edema with redness of the overlying skin. Two months after the onset of symptoms, the office of the Civil Surgeon was informed about the occurrence of an outbreak affecting the family in the village Fatehgarh. The district epidemiologist and rapid response team of IDSP of the District SBS Nagar investigated the outbreak and provided necessary medical treatment of the symptomatic cases. The clinical details of all the cases have been given in Table 1.

Nine out of 10 patients in this study presented with profuse diarrhea, accompanied by fever and restlessness in 80% of the cases. Spontaneous recurrences and remissions of bilateral pitting edema were observed in 40% cases. The overlying skin was erythematous in 7 cases (70%), which blanched on pressure. Local tenderness over the edematous limb was present in 4 cases (40%). There was no involvement of the nervous system. There were no signs of liver disease (hepatomegaly, jaundice, or other clinical signs) in any of the patients. Persistent tachycardia was observed in a single case. There were no ocular manifestations among the patients. Facial discoloration was observed in 50% of the cases, who reported topical application of the oil to hair and face. One patient who was pregnant at the time of outbreak had a still birth and the newborn was reported to have blisters on her body at the time of birth.

The adult patient who died had symptoms suggestive of cardiac involvement and died of cardiogenic shock. The other patient who was a child died of respiratory symptoms resembling pneumonia, i.e., fever and breathlessness and was being treated for pneumonia.

Laboratory investigations were done in 6 out of 8 survived cases. Three out of 6 cases tested for hemoglobin had mild (Hb 8–10 g/dL) anemia, whereas total leukocyte count and differential leukocyte count levels were normal in these cases. Blood urea was raised (> 20 mg/dL) in 50% of the cases but creatinine levels were normal. Chest-radiographs and electrocardiograms were normal. Erythrocyte sedimentation rate (ESR) was raised beyond the normal range in 5 out of 6 cases (83.3%). A female child among the patients had ESR levels above 100 mm during the first hour.

Serum samples from four of the eight patients tested positive for sanguinarine. The four patients who tested negative had comparatively mild symptoms. The concentration of sanguinarine in the samples that tested positive ranged from 0.354 to 1.169 μg/mL of serum, with a mean concentration of 0.636 μg/mL.

TABLE 1
Clinical profile of the affected patients*

Symptoms		Age and gender of the patients									
		60/F	40/M	35/F	28/M	25/F	25/M	11/M	9/M	6/F	2/M
Oedema	Legs	+	+	+	+	+	+	+	+	+	+
Constitutional symptoms	Fever	−	−	+	+	++	+++	+	++	+	+
	Restlessness	+	+		+	+	+	−	+	+	+
Cutaneous	Erythema	+	+	−	+	++	++	−	+	−	+
	Local tenderness	−	−	−	+	+	+	−	+	−	−
	Facial discoloration and hair loss	+	++	−	+++	+	+	−	−	−	−
	Oedema	−	+	+	−	+++	++	−	+	−	−
	Skin blanching	+	+	−	−	+	++	−	++	+	+
Cardiovascular system	Persistent tachycardia	−	−	+	−	−	−	−	−	−	−
	Congestive heart failure	−	−	+	−	−	−	−	−	−	−
Gastrointestinal system	Diarrhea	++	++	+++	−	++	++	+++	++	++	+
	Vomiting	−	−	+	−	−	−	+	−	−	−

*+ = Presence of the clinical sign; − = absence of the clinical sign; ++ or +++ = increase in number of + signifies increase in severity.

During the epidemiological investigation, it was found that the family was using mustard oil for cooking, which had been extracted from the local oil extraction machine in the month of June 2011. The mustard seeds were from their own cultivated land. The mustard oil samples that were being used for cooking by the affected family members tested positive for argemone oil contamination. All other samples, those from neighboring households and the one from the oil extraction machinery shop tested negative for argemone oil contamination.

Most of the patients were found to have been almost fully recovered in the follow-up examination taken by the PGIMER team after 1 year of the initial episode. Two patients complained of persistent mild skin discoloration. One patient had a systolic murmur and also complained of generalized body aches.

The District Surveillance Unit had filed the full investigation report with the National Center for Disease Control, which is a nodal agency for IDSP at national level. It also shared the findings with the local health authorities during their routine feedback meetings. Furthermore, they used this opportunity to educate the medical officers regarding unusual presentation of the epidemic dropsy so that early identification of the outbreak can be made even upon small suspicion to reduce the high case fatality rates in the future.

DISCUSSION

Dropsy is a disease that occurs in epidemics; isolated cases are seldom seen and reported.[12] Review of scientific literature could yield only two case studies reporting outbreaks restricted to a single family, although the rest of the outbreaks affected more than one family.[12,13]

The reasons for this outbreak being restricted to a particular family can only be explained if the contamination of mustard seeds with argemone seeds occurred at the household level as the mustard oil was extracted from the seeds of the plants cultivated in their own land. The negative results of the samples from all other sources support the same reasoning. Because of their low socio-economic background, the family was not aware of contamination of mustard seeds with that of argemone seeds, which had led to the current outbreak. Furthermore, the low socio-economic background also favors the use of home extracted oils, which has more chances of contamination rather than commercially available tested oils having an AGMARK sign, which is the sign for purity as per Indian standards. Various studies on epidemic dropsy from India also reported that most of the patients affected during epidemic dropsy outbreaks belong to low socio-economic status.[14–16]

In contrast to the earlier studies, the classical picture of dropsy with bilateral pitting edema, redness of skin, and breathlessness were absent. In this outbreak the main clinical symptoms reported were gastrointestinal, i.e., diarrhea and vomiting mimicking food poisoning. The onset of the symptoms was also insidious in contrast to acute onset, which is the most common presentation. Persistent tachycardia was seen in a case but without any other cardiovascular manifestations. The striking features observed in this outbreak were darkening of the facial complexion and hair loss in 50% of the cases, those who applied the oil to face and hair. This darkening might be attributed to the topical application of oil to the face, leading to transcutaneous absorption of argemone oil and sanguinarine toxicity.[14] Similar findings reporting pigmentation have been observed in other studies in the past, but facial application of the oil has not been reported.[16,17]

The clinical profile of pediatric and adult patients did not differ significantly in our study, as had been the case in a study by Gomber and others.[18] A 2-year-old male child also showed signs and symptoms, though it is usually believed that children < 2 years of age are not much affected as they ingest very few solids because of being breastfed.[19,20] The presence of symptoms among the children might be caused by an early start of weaning and solid food consumption by the children now as compared with the weaning and eating patterns seen in the 1980s and 1990s as a result of active efforts made by the Government to promote weaning at 6 months to prevent malnutrition.[21–23]

The epidemic dropsy is known to cause abortion among pregnant women because of hemangiomatous changes in the endometrium and placenta, which was also noted in the current study.[16] The mortality rate observed in the current outbreak was 20%, which is more than what was seen in earlier studies. This might be a result of late diagnosis because of misleading symptoms. The cause of deaths among the patients were cardiogenic shock caused by dilated cardiomyopathy and pneumonia.[14,16,18]

The suspicion of epidemic dropsy usually rests upon identification of some clinicoepidemiological features within a cluster of cases, which can then be confirmed by detection of argemone oil in mustard oil used for cooking.[3] The patients in this case report initially presented with gastrointestinal symptoms and being clustered to a single family presented to the health authorities as an outbreak of food poisoning/gastrointestinal illness and were treated symptomatically and the epidemic dropsy was missed. Hence, there is a need to make physicians aware that the differential diagnosis of epidemic dropsy has to be kept in mind, especially if there is a cluster of cases of repeated gastrointestinal illness within a family or neighborhood in a mustard oil consuming belt, for early diagnosis and prevention of deaths and disability among the affected members. Multisystem involvement and bilateral pitting edema seen among members belonging to the same family should also raise the suspicion of the epidemic dropsy, which was missed in this particular case, and also resulted in delayed diagnosis and deaths.

Because these cases were identified and diagnosed after a lag phase, the details of clinical symptoms and signs for the period before diagnosis were not as thoroughly recorded as should have been done. This caused the authors to restrict the study findings to those mentioned in the tables, which is an important limitation of this study.

Hence, the diagnosis of epidemic dropsy should be strongly suspected if there is repeated clustering of gastrointestinal illness cases within a single family, especially in an area consuming mustard oil.

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